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Pathology

614. **Acute Experimental Pulmonary Suppuration (Abscess and Gangrene).** (Острые экспериментальные легочные нагноения (абсцесс и гангрена))

V. H. ČIREJKIN. *Архив Патологии* [Arch. Patol.] 21, 64-70, No. 3, 1959. 5 figs., 16 refs.

The author describes experiments in which fragments of an infected embolus, produced in the femoral vein by injecting freshly collected sputum from patients with abscess of the lung, were introduced into the jugular vein of 22 dogs, in 8 of which preliminary ligation of the corresponding bronchus was performed. The pulmonary suppuration thus induced tended to take the form of an acute abscess when the embolus obstructed a relatively small vessel, but resulted in gangrene if the embolus came to rest in a larger branch of the pulmonary artery. Ligation of the bronchus alone in 3 dogs produced the expected atelectasis, but no suppuration. Acute abscesses usually resolved and the animals recovered, whereas the dogs in which gangrene developed all died. It is pointed out that the emboli used in these experiments contained a mixed flora.

A. Swan

615. **Clinical Syndromes Associated with Deficient Lung Fibrinolytic Activity. I. A New Concept of Hyaline-membrane Disease**

J. LIEBERMAN. *New England Journal of Medicine* [New Engl. J. Med.] 260, 619-626, March 26, 1959. 25 refs.

Tissue fibrinolytic activity was studied in lung and several other organs of 49 fetuses and infants dying perinatally, including 8 with pulmonary hyaline-membrane formation. The tissue activator of plasminogen was found to appear in lung as early as the third month of gestation, 33 of 41 fetuses without pulmonary hyaline-membrane formation showing this activity. However, none of the 8 infants with hyaline membranes showed this activity. Guinea pigs and rabbits—animals subject to hyaline-membrane formation from oxygen poisoning—demonstrated this same deficiency, in contrast to rats, whose lungs contained the enzyme and were more resistant to formation of the membrane. Hyaline-membrane formation was induced in guinea pigs by exposure to toxic concentrations of oxygen. This lesion appeared much more readily when oxygen poisoning was supplemented by nebulized filtered amniotic fluid.

A preliminary review of reproductive histories of mothers who delivered infants with confirmed hyaline-membrane formation shows a tendency to multiple neonatal deaths suggestive of hyaline-membrane disease.

These data suggest that a predisposing factor in hyaline-membrane formation of the newborn is the absence of

plasminogen-activator activity in lung. An interaction between amniotic-fluid or tissue thromboplastin and other clotting factors in an alveolar effusion results in deposits of fibrin that are transformed into "hyaline membrane" postnatally. Such fibrin deposits would be lysed normally through action of the fibrinolytic system if the tissue activator were present. The defect does not appear to be related necessarily to the degree of prematurity, but may represent a genetic aberration. —[Author's summary.]

CHEMICAL PATHOLOGY

616. **Experience with a Glucose-oxidase Method for Estimating Glucose in Blood and C.S.F.**

J. E. MIDDLETON. *British Medical Journal* [Brit. med. J.] 1, 824-826, March 28, 1959. 14 refs.

The ideal method of estimating the blood sugar concentration should combine specificity with economy and simplicity. The author reports, from St. Thomas's Hospital, London, the results obtained in the performance of 115 glucose tolerance tests in which he used the rapid colorimetric glucose-oxidase method described by him and Griffiths (*Brit. med. J.*, 1957, 2, 1525; *Abstr. Wld Med.*, 1958, 23, 393) which, he claims, satisfies these criteria. In 17 cases duplicate analyses were also performed by one of the more usual methods, that of MacLean, which estimates total blood reducing substances. The series included both diabetic patients and persons with normal glucose tolerance.

The values given by the two methods differed widely, the difference between them being said to represent the so-called blood saccharoid level; in 100 samples of venous or capillary blood the latter varied, apparently at random, between 0 and 81 mg. per 100 ml. with a mean of 35 mg. per 100 ml. The mean glucose level in capillary blood from the diabetic patients was significantly higher than in that from non-diabetic patients, although in venous blood from these two groups the difference was not significant. There was no correlation between the blood saccharoid and blood glucose levels. Glucose tolerance curves expressing true glucose values were obtained for normal subjects for patients with diabetes and renal glycosuria, and those showing "lag tolerance" and flat curves. As expected, these were lower than the graphs obtained by the usual method; the mean fasting level was 69 ± 13 mg. per 100 ml.

The glucose content was also estimated by the glucose-oxidase method in 29 samples of cerebrospinal fluid

(C.S.F.) and again gave lower values (50 to 76 mg. per 100 ml.) than the orthodox method; in 20 specimens of C.S.F. MacLean's method gave a saccharoid level varying from 7 to 42 (mean 19) mg. per 100 ml. It is concluded that, because of the unpredictable fluctuations in both blood and C.S.F. saccharoid levels, the use of the glucose-oxidase method in glucose tolerance tests possesses advantages over the older methods of determining blood sugar levels.

M. Sandler

617. Determination of Redox Activity of Leucocytes as a Diagnostic Aid in Systemic Lupus Erythematosus

C. D. COOPER, W. R. FELTS, T. M. BROWN, and R. H. WICHELHAUSEN. *Journal of Laboratory and Clinical Medicine [J. Lab. clin. Med.]* 53, 457-467, March, 1959. 4 figs., 23 refs.

In 1953 Chaudhuri and Martin (*J. Lab. clin. Med.*, 41, 108) demonstrated a reduction of oxidation-reduction (redox) activity in leucocytes from patients with systemic lupus erythematosus (S.L.E.) and in normal leucocytes suspended in plasma from such patients. Working at the George Washington University School of Medicine and the Veterans Administration Hospital, Washington, D.C., the present authors have studied the redox activity of leucocytes from 256 individuals, including healthy subjects and patients with various diseases. Redox activity was measured by determining the ability of the leucocytes to reduce the dye 2:6-dichlorophenolindophenol.

Depression of leucocytic redox activity was found in all of 14 cases of untreated S.L.E., with reversion to normal during steroid therapy, in 3 out of 9 cases of discoid L.E. (in all 3 of which systemic features were present, although the L.E.-cell reaction was negative), in 12 out of 21 cases of severe, febrile rheumatoid arthritis, and in all of 5 cases of the hydralazine syndrome. In 8 of the 12 cases of febrile rheumatoid arthritis with depressed redox activity S.L.E. was eventually diagnosed on the basis of the results of the L.E.-cell test or of biopsy, but at the time of testing redox activity it was difficult to distinguish these 8 from the remainder. Normal leucocytic redox activity was demonstrated in all the cases of other diseases and in the 84 healthy controls.

The authors consider the determination of leucocytic redox activity, as a diagnostic test for S.L.E., to be less subject to errors of interpretation than the L.E.-cell test, but since the former is more tedious to perform they recommend its use only in cases in which the result of the L.E.-cell test conflicts with the clinical diagnosis.

M. Wilkinson

618. Transaminases in Serum and Liver Correlated with Liver Cell Necrosis in Needle Aspiration Biopsies

S. ZELMAN and CHI CHE WANG. *American Journal of the Medical Sciences [Amer. J. med. Sci.]* 237, 323-334, March, 1959. 10 figs., 22 refs.

The serum glutamic oxalacetic transaminase (S.G.O.T.) and serum glutamic pyruvic transaminase (S.G.P.T.) levels are often increased in patients with various diseases of the liver. It has been suggested that these increases are due to release of the enzymes as a

result of liver cell necrosis. From the Veterans Administration Hospital, Topeka, Kansas, the authors report the results of 143 needle biopsy examinations of the liver in 108 cases of proven or suspected disease of this organ. The extent of hepatic necrosis, as estimated on histological grounds and graded from 0 to 3, was then compared with the S.G.O.T. and S.G.P.T. values determined on the day of biopsy. In 25 cases additional liver tissue was obtained (at the same time and site) for estimation of tissue transaminase activity.

In the 130 instances in which S.G.O.T. values were available these correlated closely with the grade of necrosis: thus all 38 biopsy specimens graded as normal were associated with a normal S.G.O.T. level, that is, less than 40 units per ml., the mean value for the group being 19 units per ml.; of 70 specimens in Grade 1, the S.G.O.T. value was normal in 61 (87%) and in none was it over 94 units per ml. (mean 25 units per ml.); of 17 in Grade 2 (moderate necrosis), 12 (71%) were associated with high S.G.O.T. levels (mean value 77 units per ml.), while all 5 specimens in Grade 3 were associated with high S.G.O.T. values (mean 166 units per ml.). The S.G.P.T. values, available in only 50 cases, also correlated with the grade of necrosis, the means being 19, 39, 54, and 211 units per ml. for Grades 0, 1, 2, and 3 (normal value 35 units per ml.).

The 25 liver tissue G.O.T. and the 13 tissue G.P.T. estimations revealed an inverse relationship to the degree of necrosis of liver cells for both enzymes. The tissue transaminase levels were determined per mg. of total liver tissue in the biopsy specimen (about 50 mg.), no account being taken of fat or fibrous tissue present. To confirm that the trauma of liver needle biopsy had not itself caused a rise in transaminase levels the S.G.O.T. value was determined again in the first 20 patients on the day following biopsy; no significant difference was found in any of these patients. The authors conclude that this study "not only confirms the serum estimation of the transaminases as a fairly reliable index of necrosis in the diseased liver, but also lends confidence to the appraisal of histologic evidence of necrosis in representative liver biopsy specimens obtained by needle aspiration".

I. Berkinshaw-Smith

MORBID ANATOMY AND CYTOLOGY

619. Neuropathologic Observations in Phenylketonuria

C. M. POSER and L. VAN BOGAERT. *Brain [Brain]* 82, 1-9, March, 1959. 11 figs., 26 refs.

Since very few detailed pathological reports have been published on the cerebral changes in patients with phenylketonuria a detailed case report is here presented from the University of Kansas and the Institut Bunge, Antwerp, of a boy who was first noted to have behavioural peculiarities and retarded mental development at the age of 6 years, when he entered school. He was first seen by the authors at the age of 7½; his I.Q. then was 30, he had a severe speech defect, suffered from frequent fits which were resistant to therapy, and had had several episodes of status epilepticus. When examined

again at the age of 14½ his mental age was 4½ years (I.Q. 36). He died at the age of 18 following a convulsion. Detailed neuropathological examination showed pallor of the myelin sheath in well defined areas along the fibre tracts involved, particularly the subcortical bundles, the corpus callosum, the paraventricular bundles, the cerebellar white matter, the hilum of the dentate nuclei, and the optic tract. These changes were accompanied by severe gliosis. Very little evidence of active catabolism of myelin or breakdown products could be found.

Comparison of these findings with those in other reported cases led the authors to conclude that (1) the changes observed in these cases are old and quiescent; (2) there is probably some interference with the metabolic activities concerned with the formation of myelin during the first 2 or 3 years of life, and the condition may be looked upon as analogous to the dysmyelination found in the cerebral lipidoses and the leucodystrophies. No significant changes were encountered in the nerve cells. The relevant literature is reviewed at some length.

J. B. Cavanagh

620. Criteria of Thymic Cancer and Clinical Correlations of Thymic Tumours

G. D. ANDRITSAKIS and S. C. SOMMERS. *Journal of Thoracic Surgery* [J. thorac. Surg.] 37, 273-290, March, 1959. 17 figs., 42 refs.

In this paper from the Massachusetts Memorial Hospitals and the University School of Medicine, Boston, the histological features of 50 tumours considered to be of thymic origin are described and the clinical data are reviewed. About two-thirds of the tumours were carcinomata or adenomata. Pressure symptoms predominated in 20 of the 50 patients; of the remainder, 20 were asymptomatic, 7 had myasthenia gravis, 2 had aregenerative anaemia (in one of whom agammaglobulinaemia later developed), and one had Cushing's syndrome. Correlation of the pathological findings with the clinical features showed that where there were vacuolated or hydropic cells in abundance "a likelihood of myasthenia gravis might be inferred".

The physiology of the thymus is discussed with reference to the findings.

J. B. Wilson

621. Renal Lesions in Scleroderma: Clinical and Pathological Features

J. D. TANGE. *Australasian Annals of Medicine* [Aust. Ann. Med.] 8, 27-34, Feb. [received April], 1959. 11 figs., 29 refs.

The author describes, from the Department of Pathology, University of Melbourne, the renal lesions in 3 cases of scleroderma occurring in females aged 36, 46, and 69 years respectively. All 3 patients died of renal failure between 1 and 2 years from the onset of the disease. He has also collected, and presents in a table, the relevant details of 34 similar cases reported in the literature.

The significant renal lesion is a mucoid and loose fibrous swelling of the walls of the intralobular arteries without inflammatory reaction, the arterial lumen being narrowed or obliterated. This interference with the

blood flow leads to focal cortical infarcts. The appearances of the renal lesion and the clinical course of the disease are almost identical with those described in malignant hypertension. The administration of adrenal corticosteroids is not recommended in the treatment of scleroderma, since in a number of reported cases of this disorder these drugs have appeared to accelerate the progress of the hypertension or even to determine its appearance.

A. W. H. Foxell

622. Subclinical *Pneumocystis* Pneumonitis

W. H. SHELDON. *A.M.A. Journal of Diseases of Children* [A.M.A. J. Dis. Child.] 97, 287-297, March, 1959. 9 figs., 24 refs.

This paper from Emory University School of Medicine, Atlanta, Georgia, describes in detail 2 cases in which pneumonitis due to *Pneumocystis carinii*, but lacking many of the typical features of fully developed interstitial plasma-cell pneumonia, was encountered incidentally at necropsy.

The first patient was a 3-month-old girl who was found dead in her cot without previously having shown any significant signs of illness. Macroscopically, all the organs and tissues appeared normal with the exception of the lungs, which were slightly increased in weight and mildly consolidated. Histological examination showed the presence of foci of interstitial pneumonitis with infiltration of the septa by lymphocytes, occasional plasma cells, and large mononuclear cells. In these areas the cells lining the alveoli were prominent and were frequently seen lying free in the alveolar lumen, singly or in small aggregates. There was no "honeycomb" material, nor were giant cells or hyaline membranes observed. The alveoli contained small numbers of *Pneumocystis* cysts, with fewer free forms, which frequently appeared to be in close contact with the cells of the alveolar lining cells and the intraluminal cells, but were not seen within them or in the septa. They were readily demonstrable with Giemsa stain, Gomori's methenamine silver, or the periodic-acid-Schiff technique. *Staphylococcus aureus* was cultivated from the lung tissue, but mycological culture of fresh-frozen tissue a few weeks after necropsy was unsuccessful. The cause of death was considered to be a fulminant staphylococcal infection. The second patient was a girl of 10 who died of cerebral haemorrhage following glomerulonephritis. At necropsy the lungs showed the same histological appearances as in the first case, but here rare multinucleated giant cells were present in the alveoli. Small numbers of *Pneumocystis* organisms, mostly cysts, were again found in the alveoli in close contact with the alveolar-lining cells, but not within the cells or in the septa. Culture was impracticable.

The unusually mild degree of the *Pneumocystis* infection in these cases is stressed, and it is suggested that latent and subclinical infections, with focal, non-progressive lesions, may occur not infrequently in the U.S.A., where clinically manifest *Pneumocystis* pneumonia of the European type is rarely seen.

(Two further cases of subclinical *Pneumocystis* pneumonitis are briefly reported in an addendum.)

F. Hillman

Microbiology and Parasitology

623. **Electron-microscopical Investigation of Diphtheria Bacteriophages.** (Электронномикроскопическое изучение дифтерийных бактериофагов)

V. V. POSPELOVA. *Журнал Микробиологии, Эпидемиологии и Иммунологии* [Ž. Mikrobiol. (Mosk.)] 30, 40-44, Feb., 1959. 9 figs., 5 refs.

At the Gamalaya Institute for Epidemiology and Microbiology, Moscow, 5 different strains of diphtheria bacteriophage were examined with the electron microscope to discover any morphological differences. Such differences were thought to be possible because the bacteriophages all differed in respect of their sensitivity to inactivating substances, antigenic structure, and speed of absorption by sensitive diphtheria strains.

As was shown in the only other published electron-microscopical investigation of diphtheria phages known to the author (Freeman, *J. Bact.*, 1951, 61, 675) the phage structure was found to be similar to that of the phage of *Escherichia coli*; it consisted in a round head 66 mμ in diameter and a narrow, cylindrical tail 260 to 270 mμ in length. A few single phage cells were seen (and are illustrated) which had ovoid or double heads, but all attempts to isolate daughter phage strains with a different morphology were unsuccessful. Diphtheria phages appear to act only slowly on their hosts, since after 5 hours of contact a great number of cells of *Corynebacterium diphtheriae* were still unaltered. The harvest of diphtheria phage is higher than would be expected if only a single multiplication cycle were involved.

K. Zinnemann

624. **Study of Far Eastern Strains of Pathogenic Leptospirae of New Serological Types.** (Результаты изучения дальневосточных штаммов патогенных лептоспир новых серологических типов)

N. N. KRAMINSKAJA. *Журнал Микробиологии, Эпидемиологии и Иммунологии* [Ž. Mikrobiol. (Mosk.)] 30, 54-58, Feb., 1959. 1 fig., 10 refs.

Leptospirae are of frequent occurrence in man and domestic animals in the Far Eastern provinces of the U.S.S.R., and numerous investigations of the organisms responsible have been carried out. In this paper two new serological types of *Leptospira* are described as occurring in man. One of these, *L. muris*, was first isolated by the author in 1956 from white mice, while the other is named *L. ussuri*. Cross-agglutination tests have been carried out with *L. hebdomadis*, *L. sejroe*, and *L. saxkoebing*. Serologically, the two new types seem to be related, but they are not identical as cross-agglutinations do not occur to full titre, the agglutination titres with the three recognized types being at best one-tenth of the maximum. On this basis the claim is made for their recognition as new serological types.

[It will be recalled that until recently Soviet workers made similar claims for *L. monjakov*, also originally

found in the Far Eastern provinces, which has now been shown to be identical with *L. pomona*. The two new types now reported have a similarly spurious investigational basis, and for the time being the author's claims must be viewed with caution.]

K. Zinnemann

625. **Observations on a Chemical Test Related to the Virulence of *Staphylococcus aureus***

D. M. MYERS. *American Journal of Clinical Pathology* [Amer. J. clin. Path.] 31, 128-132, Feb., 1959. 7 refs.

This paper from the U.S. Naval Medical School, Bethesda, Maryland, describes the use of ammonium molybdate in a chemical test for the detection of pathogenicity in cultures of *Staphylococcus aureus*. This A.M.C. (ammonium molybdate chemical) test "apparently detects an enzyme system, but not the coagulase or the phosphatase systems", and it is suggested that it provides "an indirect measurement of the amount of hyaluronidase produced by the organism". It is performed on a plasma culture of the strain to be tested, a positive result being denoted by the development of a blue colour of an intensity which varies with the pathogenicity of the organism. [For details of the technique and the materials used the original paper should be consulted.]

No correlation was found between the results of the A.M.C. test and the coagulase reaction with 156 haemolytic strains of *Staph. aureus* isolated from routine hospital material, nor was there any correlation with mannitol fermentation in 106 cultures. The source of the organism tested and its sensitivity to 16 different antibiotics and antibacterial agents were also found to bear no relation to the results of either the A.M.C. test or the coagulase reaction in 220 cases. The results of the coagulase and mannitol fermentation reactions and of the A.M.C. test on 20 strains of *Staph. aureus* were then compared with their pathogenicity on injection into white mice. The result of the A.M.C. test showed the closest correlation with pathogenicity, as indicated either by the mortality among the infected mice or by the ease with which the infecting organism was recoverable from the organs, though none of the tests was infallible. The A.M.C. test was then performed on cultures of staphylococci from patients with local and with systemic infections, and a close association was found between the invasiveness of the organism and its reaction to the A.M.C. test. Thus 36 of 45 strains isolated from local infections gave a negative A.M.C. reaction, whereas all of 24 strains causing systemic infections gave a positive reaction. The relation of the coagulase and mannitol fermentation reactions of these strains to their invasiveness was less marked.

The author concludes that the A.M.C. test provides a better guide to the pathogenicity of staphylococci than the other tests studied. The mechanism of the reaction

is discussed and evidence is presented which suggests that the amount of hyaluronidase produced by an organism plays an important part in determining its virulence.

I. Berkinshaw-Smith

SEROLOGY AND IMMUNOLOGY

626. A Bentonite Flocculation Test for the Diagnosis of Hydatid Disease in Man and Animals

L. NORMAN, E. H. SADUN, and D. S. ALLAIN. *American Journal of Tropical Medicine and Hygiene* [Amer. J. trop. Med. Hyg.] 8, 46-50, Jan., 1959. 8 refs.

At the U.S. Public Health Service, Communicable Disease Center, Atlanta, Georgia, the bentonite flocculation (B.F.) test previously used for the diagnosis of trichinosis was adapted as a serological technique for the diagnosis of hydatid disease and its efficacy evaluated in 6,689 samples of serum. Antigens were prepared from hydatid fluid from which salts were removed by dialysis and the volume then reduced to one-third of the original by preevaporation. Antigen was also prepared by three different methods as extracts of scolices obtained from hydatid sand: for antigen Type A washed scolices were extracted with normal saline; for Type B lyophilized scolices were substituted for the wet material; and for Type C the lyophilized scolices were treated with ether before extraction to prepare a fat-free antigen. The antigens were adsorbed on to standard-sized bentonite particles and the tests were carried out by addition of this material to serially diluted serum. If more than 50% of particles were flocculated after 15 minutes the reaction was considered positive. Control complement-fixation (C.F.) tests were carried out with standard hydatid-fluid antigen. Positive control sera for all tests were obtained from a limited number of proved cases of hydatid disease in human beings. Other specimens of serum were from symptomatic cases and from patients suffering from other diseases. Negative control sera were obtained from healthy Service personnel.

Comparison of the results obtained with the C.F. and B.F. tests showed that the latter gave more positive reactions and suggested that reactions below a titre of 1:10 might be non-specific. It is considered that of the various antigens employed, those prepared from scolices may be more specific than those from hydatid fluid. The test is regarded as of practical value.

O. D. Standen

627. An Evaluation of the Hemagglutination and Flocculation Tests in the Diagnosis of Echinococcus Disease

I. G. KAGAN, D. S. ALLAIN, and L. NORMAN. *American Journal of Tropical Medicine and Hygiene* [Amer. J. trop. Med. Hyg.] 8, 51-55, Jan., 1959. 12 refs.

Specimens of serum from patients suffering from a wide variety of diseases, including 30 specimens from clinically diagnosed cases of echinococcosis, were used for a comparative evaluation of the tannic acid haemagglutination (H.A.), the bentonite flocculation (B.F.), and the complement-fixation (C.F.) tests. The antigens were prepared by standard methods. Of 30 specimens

of serum from clinically verified cases, the H.A. test gave a positive reaction in 29 and the B.F. test a positive reaction in 27; the response to the C.F. test was positive in only 8 out of 22 sera. Of 246 cases of other diseases, 14.2% gave a false positive reaction to the H.A. test and 10% a false positive reaction to the B.F. test. It is considered that positive reactions to the H.A. and B.F. tests in sera from clinically diagnosed cases of echinococcosis constitute presumptive evidence of infection with *Echinococcus*.

O. D. Standen

628. A Correlative Study of Immunological Tests for the Diagnosis of Hydatid Disease

G. A. GARABEDIAN, R. M. MATOSSIAN, and F. G. SUIDAN. *American Journal of Tropical Medicine and Hygiene* [Amer. J. trop. Med. Hyg.] 8, 67-71, Jan., 1959. 13 refs.

A correlative study of the 3 immunological tests, complement fixation, indirect hemagglutination and intradermal tests was carried out on 79 patients with hydatid disease and 105 patients with miscellaneous conditions. The mean percentages of positive reactors among the 79 patients with hydatid disease tested by complement fixation, intradermal and indirect hemagglutination tests, were, respectively, 77.2, 88.6 and 87.3. Among the 105 patients with conditions other than hydatid disease the percentages of positive results were 5.9 in complement fixation, 18.1 in intradermal and 0 in indirect hemagglutination tests. On the basis of these findings it may be stated that indirect hemagglutination as applied for the diagnosis of hydatid disease is a more specific test than are complement fixation and intradermal tests.—[Authors' summary.]

629. Use of Gel Diffusion Precipitation Test in the Diagnosis of Adenovirus Infections

M. S. PEREIRA, H. G. PEREIRA, and A. C. ALLISON. *Lancet* [Lancet] 1, 551-552, March 14, 1959. 12 refs.

In this study of methods of diagnosis of adenovirus infections the authors, working at the Virus Reference Laboratory and the National Institute for Medical Research, London, used Ouchterlony's agar-gel diffusion precipitation test for the detection of adenovirus antibodies, the antigen being a preparation of adenovirus Type 5 obtained from HeLa-cell cultures and partially purified by the fluorocarbon compound technique of Gessler *et al.* (As a simplification of the method applicable to diagnostic work it was found that equally satisfactory antigens could be obtained by freezing and thawing, or by grinding, the virus-infected HeLa-cells.) Representative tests, illustrated diagrammatically, showed that precipitation lines occurred between the adenovirus antigen and samples of serum derived from a rabbit immunized with adenovirus Type 5 and from 2 patients convalescing from infections with adenovirus Types 3 and 5 respectively. The reactions demonstrated the similarity of the antibodies in the three sera and the group-specificity of the reaction. Negative results were given with acute-phase sera from the same 2 patients and with a HeLa-cell rabbit antiserum.

Tests performed on miscellaneous human sera showed that the results of the gel-diffusion precipitation test were closely related to those of the complement-fixation test; positive precipitation reactions were obtained with the great majority of sera having complement-fixation titres higher than 1:80, but with very few of the sera of lower titre. In tests on 26 paired acute-phase and convalescent-phase sera from cases of adenovirus infection, positive precipitation reactions were obtained in 24 of the convalescent-phase sera, but in only 4 of the acute phase-sera, and in these the reaction was delayed.

Further work is being undertaken in an attempt to explain the occasional appearance of precipitation lines in plates observed for longer than the usual 2-day period with sera previously giving a negative result, and also the occurrence with some sera from immunized animals or from infected persons of more than one precipitation line.

The authors consider that the simplicity of the test suggests that it would be of value in the routine diagnosis of adenovirus infections.

Joyce Wright

630. The Morphological Basis of Antibody Formation Development during the Neonatal Period

R. A. BRIDGES, R. M. CONDIE, S. J. ZAK, and R. A. GOOD. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 53, 331-357, March, 1959. 12 figs., 36 refs.

This paper from the Pediatric Research Laboratories of the Variety Club Heart Hospital, Minneapolis, is divided into four parts. The first describes a study carried out on a normal child born of a woman with acquired agammaglobulinaemia. An antigen (T.A.B. vaccine) was injected subcutaneously at the age of 2 days, then weekly up to the age of 2 months, and thereafter monthly until the age of one year. The serum was examined at intervals for the presence of agglutinins against typhoid antigens and of isoagglutinins to heterologous blood groups (the child being of Group O), and the serum γ -globulin level was determined by an immunochemical method and by estimation of the total protein by the standard Biuret technique together with paper or free moving boundary electrophoresis. Lymph-node biopsy was performed on three occasions. During the neonatal period all the findings were those of agammaglobulinaemia. At about the 6th week the serum γ -globulin level began to rise and at the same time typhoid antibody (H component) became demonstrable. At 3 months of age the serum γ -globulin level was normal, plasma cells had appeared in the lymph nodes, and agglutinins to the H, O, and B antigens of T.A.B. and isoagglutinins to erythrocytes of Groups A and B were demonstrable in the blood. Thus the agammaglobulinaemia which was apparently present for the first 6 weeks of life had disappeared by the time the infant was 3 months old.

The second part reports the absence of plasma cells from the bone marrow of 20 normal children aged one to 5 days, while the third part reports a similar lack of plasma cells in the lamina propria of the appendix and the ileum in all but one of 15 children less than one

month of age and their presence in these situations in children aged 6 months and upwards.

The fourth part of the paper describes experiments in which litters of rabbits of different ages were divided into three groups, one serving as a control group and the others receiving injections of different preparations of crystalline bovine serum albumin (B.S.A.) into the hind feet. It was shown that injection of a saline solution of B.S.A. did not precipitate any plasma-cell response in the lymph nodes or antibody response in the blood in animals younger than 28 days. With the more intense antigenic stimulus provided by incorporating the B.S.A. in Freund's adjuvant (a water-in-oil emulsion containing *Mycobacterium butyricum*), however, a morphological reaction was observed at the 16th day and antibody production at the 16th day of life in animals inoculated at the age of 7 days.

The authors discuss their findings and suggest that the immunological defence mechanisms come into action during the second month of life in the normal child and that this can be correlated with the appearance of plasma cells in the lymph nodes and other tissues. They suggest further that the condition of congenital agammaglobulinaemia is a disease in which the normal neonatal "immunologically null period" is prolonged indefinitely.

A. E. Wright

631. Significance of Experimental Kerato-conjunctivitis as a Model for the Study of Immunity in Dysentery.

(Значение экспериментального керато-конъюнктивита как модели для изучения иммунитета при дизентерии)

N. A. JAHNINA and N. S. KUZNECOVA. *Журнал Микробиологии, Эпидемиологии и Иммунологии* [Zh. Mikrobiol. (Mosk.)] 30, 98-102, Feb., 1959.

In 1955 Seren reported that the inoculation of freshly isolated strains of dysentery bacilli into the eyes of guinea-pigs caused a specific kerato-conjunctivitis. In a study carried out at the Gamalaya Institute, Moscow, this method has now been verified and extended to all known pathogenic dysentery organisms, including *Shigella shiga*, *Sh. schmitz*, *Sh. boyd*, *Sh. sonnei*, and *Sh. newcastle*. Inoculation with *Salmonella typhosa*, *S. paratyphosa*, *Escherichia coli*, and *Proteus vulgaris* did not induce a similar kerato-conjunctivitis. The technique is simple; with a wire loop 2 mm. in diameter roughly 500 million organisms are inoculated under the upper and lower eyelids, using a 24-hour culture of a freshly isolated strain. The pathological changes, which start after one to 3 days, may last from one to 6 months or longer and lead to opacity of the cornea. The infecting organism can be isolated from the purulent conjunctival discharge during the whole inflammatory period. Old laboratory strains did not cause similar lesions. The eye infection leads to the formation of specific agglutinins in the blood with titres up to 1:800, and to specific immunity to reinfection which lasts for 2 to 6 months. There is no cross-immunity between the dysentery species. Of the various organisms tested, *Sh. flexneri* caused the most severe kerato-conjunctivitis.

K. Zinnemann

Pharmacology and Therapeutics

632. The Effect of Dosage Forms on the Duration and Continuity of Action of Belladonna Alkaloids

D. R. REESE, S. M. FREE, J. V. SWINTOSKY, and M. I. GROSSMAN. *American Journal of Digestive Diseases* [Amer. J. dig. Dis.] 4, 220-228, March, 1959. 13 refs.

At the Veterans Administration Center, Los Angeles, a clinical trial was undertaken to evaluate the pharmacological action of a sustained-release preparation of belladonna alkaloids dispensed in the form of a "spansule", that is, a capsule containing hundreds of minute, lipid-coated spheroids of the drug which, after ingestion, disintegrates to release the medication over an extended period. The trial was carried out on 8 ambulatory female in-patients ranging in age from 39 to 77 years. [The conditions for which they were under treatment are not stated.] Each patient was allowed to become familiar with the Mushin salivary suppression test, a modification of which was used subsequently to assess the anticholinergic effect of the preparation under trial. The study was a double-blind one, patients being allocated to the various test regimens by the "latin square" design and each acting as her own control; the details of administration of the preparations were planned to allow statistical evaluation of the results. Three different dose levels of the sustained-release preparation were compared with 4-hourly administration of a non-sustained-release preparation and with a placebo capsule. An interval of one to 3 days was allowed between individual tests.

The action of the non-sustained-release capsule was clearly distinguished from that of the placebo and was complete in less than 6 hours. The action of the sustained-release form lasted for about 12 hours, and its effect was devoid of the "peaks and valleys" which are often observed with intermittent administration of ordinary pharmaceutical preparations. Thus a single spansule will produce a smooth continuous effect, with the advantage that such effect will last overnight.

T. J. Thomson

633. Comparative Effect of Phenaglycodol, Meprobamate, and a Placebo on the Irritable Colon

A. M. KASICH, H. D. FEIN, and J. W. MILLER. *American Journal of Digestive Diseases* [Amer. J. dig. Dis.] 4, 229-234, March, 1959. 16 refs.

From the Lenox Hill Hospital, New York, the authors describe a double-blind clinical trial of the effects of a placebo, meprobamate, and "phenaglycodol" (2-p-chlorophenyl-2:3-butanediol) on 135 selected patients suffering from chronic irritable colon. Phenaglycodol is a recently synthesized tranquilizer which is reported to have a selective action on the thalamus rather than on the cerebral cortex. The 72 women and 63 men studied, whose ages ranged from 19 to 64 years, were divided at random into three equal groups, each of which was given one of the drugs or the placebo in a capsule thrice

daily after meals for 2 to 4 weeks. All the patients were maintained on a bland diet and received no additional medication during the period of trial. Each patient was asked to comment daily in writing on the number and consistency of bowel movements, the presence of abdominal distension or cramps, and to record any side-effects, and at the end of the trial to state whether the capsule had influenced the disorder.

Statistical analysis of the results showed that both meprobamate (400 mg.) and phenaglycodol (300 mg. daily) were more effective than the placebo, but there was no significant difference between the effects of the active drugs. Side-effects, including drowsiness, nausea, vomiting, and diarrhoea were most common in patients taking the placebo. The authors conclude that tranquilizers like phenaglycodol and meprobamate are of value in helping patients with irritable colon temporarily to overcome tension, which is considered to be one of the chief aetiological factors in this condition. T. J. Thomson

634. Less Commonly Recognized Actions of Atropine on Cardiac Rhythm

K. H. AVERILL and L. E. LAMB. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 237, 304-318, March, 1959. 9 figs., 18 refs.

This paper from the School of Aviation Medicine of the U.S. Air Force, Randolph Base, Texas, draws attention to certain changes in cardiac rate, rhythm, and conduction induced by the administration of atropine in addition to the tachycardia resulting from its vagus-blocking effect. Atropine sulphate was given intravenously in doses of 0.8 to 1.2 mg. to 60 patients under examination for a clinical syncopal episode, 50 normal subjects serving as controls for the evaluation of syncopal reactions, and to more than 100 patients with various types of cardiac arrhythmia. Electrocardiograms (ECGs) were recorded continuously from the moment of injection to the time of establishment of full atropinization, special attention being paid to the period from 30 to 90 seconds after the injection, during which the initial vagotonic effect of the drug is replaced by its final prolonged vagolytic effect. During this period various transient arrhythmias were observed, which are described in some detail. They included A-V dissociation with interference, with synchronization, with lower atrial rhythm, and with "ventricular parasystole", the appearance of an ectopic atrial rhythm, and second-degree A-V block. Changes in the ECG in a case of Wolff-Parkinson-White syndrome are also described.

It is stated that between the initial vagotonic phase of the action of atropine and its eventual vagolytic phase there is a period of "vagal imbalance" during which changes in cardiac rhythm occur resembling those which can be produced by various respiratory procedures. Although the cardiac effects of atropine in normal doses are harmless, serious disturbances of rhythm may occur

if it is given in combination with other drugs, such as neostigmine, particularly in patients under cyclopropane anaesthesia.

A. Schott

635. A Comparative Study of the Saluretic and Diuretic Effects of Hydrochlorothiazide and Chlorothiazide. (Étude comparative de l'action sali-diurétique de l'hydrochlorothiazide et du chlorothiazide)

C. BARTORELLI, N. GARGANO, and A. ZANCHETTI. *Schweizerische medizinische Wochenschrift* [Schweiz. med. Wschr.] **89**, 331-334, March 21, 1959. 12 refs.

This paper from the University of Sienna describes a comparative trial of the diuretic sulphonamides chlorothiazide and hydrochlorothiazide on 5 normal subjects who were maintained on a diet of fixed calorie, water, and mineral content. The doses of chlorothiazide given ranged from 250 to 2,000 mg. and those of hydrochlorothiazide from 3.125 to 200 mg. Each drug was given in single doses at 5-day intervals and the subsequent excretion of sodium, potassium, chloride, bicarbonate, and water was measured.

The effect of hydrochlorothiazide on the excretion of sodium was found to be about 40 times, of chloride and water 50 times, of potassium 30 times, and of bicarbonate twice as great as that of chlorothiazide. Hydrochlorothiazide also had a more prolonged action than the parent substance and differed from it in its pattern of activity, which closely resembled that of the organic mercurials.

G. S. Crockett

636. Observations on the Use of Flumethiazide in the Treatment of Edema

J. B. ROCHELLE, A. C. MONTERO, and R. V. FORD. *Antibiotic Medicine and Clinical Therapy* [Antibiot. Med.] **6**, 267-271, May, 1959. 3 figs., 2 refs.

Flumethiazide [6-(tri-fluoromethyl)-1:4:2-benzothiadiazine-7-sulfonamide-1:1-dioxide] appears to be a potent natriuretic and diuretic agent when administered orally. There is no significant difference in its potency when compared to chlorothiazide. The drug is repetitively effective and is associated with no significant derangement of the biochemical architecture. It is of value in the treatment of edema of varied etiology, including the edema of pregnancy, nephrotic edema, and cirrhotic edema.—[Authors' summary.]

637. Clinical Study of a New Synthetic Non-barbituric Hypnotic, Propynylcyclohexanol Carbamate. (Étude clinique d'un nouvel hypnotique non barbiturique de synthèse, le carbamate de propynylcyclohexanol)

C. LAROCHE, F. CHAIN, and N. T. KY. *Presse médicale* [Presse méd.] **67**, 449-450, March 7, 1959. 3 refs.

The authors, writing from the Hôpital Broussais, Paris, report a clinical trial of a new non-barbiturate hypnotic—propynylcyclohexanol carbamate (L. 2103). In preliminary experiments on mice it was shown that the drug rapidly induced hypnosis of considerable duration and that it had a very favourable therapeutic index. It did not cause excitation before hypnosis and it had only a slight depressive action on the cardiovascular and respiratory systems.

The clinical trial was carried out in 170 patients (74 men and 96 women) admitted to hospital for various disorders and complaining of insomnia, those selected being usually unable to sleep for more than 3 hours. The dose given varied between 200 and 600 mg., the effective dose being generally about 400 mg. The results obtained with a dose of 400 mg. were as follows: very good (8 to 10 hours' calm sleep), 35 patients (20.6%); good (6 to 8 hours' calm sleep), 80 patients (47%); fair (4 to 6 hours' calm sleep), 26 patients (15.4%); and negative (less than 3 hours' calm sleep), 29 patients (17%). Thus 115 patients (67.6%) were regarded as responding satisfactorily to this dose, with more than 6 hours' calm sleep, while a number of others responded well to a higher dose (600 mg.). Of the 29 patients who failed to respond, 11 were suffering from severe pain due to conditions such as cancer or herpes zoster. The authors also emphasize that the trial was carried out in the wards of a general hospital, where conditions were not always conducive to rest. Only in one case did the drug appear to have no hypnotic action; in none did it cause dreaming or excitation. Satisfactory sedation during the day was obtained in a few cases with 200 to 600 mg. daily in divided doses.

In order to eliminate the factor of patient suggestibility comparative trials were carried out with L. 2103 and a placebo (lactose). The active drug and the placebo were administered by the double-blind method on alternate nights to 21 patients, 18 of whom responded equally satisfactorily to both. When L. 2103 was given to 13 patients for several successive nights and then replaced by the placebo the hypnotic effect was fully maintained with the placebo in 7 cases, while 2 patients were affected by neither product and 4 by L. 2103 only. This seemed to indicate that normal sleep might be restored in many cases after the administration of the hypnotic for a few nights only. Comparative trials were also carried out with butobarbitone, methylpentynol, and glutethimide on 48 patients. When 100 mg. of butobarbitone and 400 mg. of L. 2103 were given on successive nights to 17 patients, the order of administration being varied, L. 2103 was the more effective in 5 cases and butobarbitone in 5, the effects being identical in the remaining 7 cases; under the same conditions the effect of 400 mg. of L. 2103 was found to be equal or superior to that of 250 mg. of methylpentynol in 19 out of 21 cases. A dose of 200 to 400 mg. of L. 2103 was found to be comparable in effect to 250 to 500 mg. of glutethimide in 10 patients to whom the drugs were administered alternately for a period of 8 days.

L. 2103 was given to many patients continuously for several weeks without loss of effect, an increase in dose being found necessary in less than 10% of cases. The drug produced no drowsiness or headache on waking, no toxic or allergic side-effects or haematological changes were noted, and no adverse effects on the liver or kidneys were detected by hepatic and renal function tests [on an unspecified number of subjects].

The authors conclude that L. 2103 seems to be at least as effective as the best hypnotics available at present, and to be devoid of all toxicity in therapeutic doses.

P. T. Main

Chemotherapy

638. Clinical Experience with a New Erythromycin Derivative, Erythromycin Propionate: Report of One Hundred Five Cases

I. M. SMITH and W. H. SODERSTROM. *Journal of the American Medical Association* [J. Amer. med. Ass.] 170, 184-188, May 9, 1959. 10 refs.

The authors report the results of a trial of erythromycin propionate, which is absorbed more rapidly and produces higher peak concentrations than erythromycin, in the treatment of 105 patients at Iowa State University Hospitals, Iowa City. The ages of the patients ranged from 6 to 89 years and the conditions treated included pustular acne, furuncles, carbuncles, other staphylococcal skin infections, osteomyelitis, and staphylococcal infections of the respiratory tract. The drug was administered orally in capsules in a dosage of 0.25 or 0.5 g. four times a day and treatment was continued over periods ranging from several days to 2 months, the average duration being 12 days.

A satisfactory response occurred in 98 (94%) of the patients, 10 of whom had previously failed to respond to other forms of chemotherapy. Gastro-intestinal side-effects occurred in only 8 patients and were mild. There were no toxic effects on the liver, kidneys, or blood, and no allergic reactions developed. The authors conclude that erythromycin propionate is an effective drug in treating many common conditions due not only to staphylococcal infection, in which it is particularly efficacious, but also to streptococcal and pneumococcal infection, that its side-effects are mild and infrequent, and that superinfection does not occur.

Gerald Sandler

639. The Sensitivity of Staphylococci and Other Wound Bacteria to Erythromycin, Oleandomycin, and Spiramycin

E. J. L. LOWBURY and L. HURST. *Journal of Clinical Pathology* [J. clin. Path.] 12, 163-169, March, 1959. 2 figs., 10 refs.

Staphylococci isolated from patients are often described as resistant to one member of the erythromycin group of antibiotics but sensitive to another; this has been termed "dissociated resistance". In this paper from the Birmingham Accident Hospital an investigation is reported of the incidence of dissociated and cross-resistance in 620 strains of *Staphylococcus aureus* isolated from burns during one month in 1957 and tested by the ditch plate method for sensitivity to erythromycin, oleandomycin, and spiramycin. Of the 267 strains sensitive to erythromycin, all were sensitive to oleandomycin when examined after incubation for 18 hours and all except 5 were still fully sensitive after 42 hours' incubation; 265 were sensitive to spiramycin. Of the 353 strains resistant or only slightly sensitive to erythromycin, only 36 were fully sensitive to oleandomycin

after 18 hours' incubation, 211 showed some resistance, and 106 were fully resistant; after 42 hours' incubation only 5 strains were still fully sensitive, 59 showed some resistance, and 289 were fully resistant. With spiramycin, as with other antibiotics, this phenomenon of delayed growth was not observed, 259 of the erythromycin-resistant strains being sensitive after 18 hours' incubation and 258 after 42 hours.

Growth curves showed that the erythromycin-resistant, oleandomycin-sensitive strains began to multiply in the presence of oleandomycin after about 24 hours' lag, during which the number of viable organisms fell. Phage typing indicated that the sensitive strains included a larger proportion of strains of Phage Group II, while resistant and dissociating strains showed various phage patterns belonging to Group III. Mouse protection tests suggested that oleandomycin and even erythromycin might have some therapeutic action against staphylococci showing dissociated resistance to erythromycin, but the action was less than that of spiramycin against these strains or that of any of the erythromycin group against fully-sensitive strains. Against *Clostridium welchii* oleandomycin was the least active, while against *Streptococcus pyogenes* both oleandomycin and spiramycin seemed to have about the same bacteriostatic activity.

A. Ackroyd

640. Sulfaphenazol (Orisul), a Long-acting Antibacterial Sulfonamide

W. P. BOGER. *Journal of the American Geriatrics Society* [J. Amer. Geriat. Soc.] 7, 314-321, April, 1959. 3 figs., 10 refs.

From Norristown State Hospital, Pennsylvania, a comparative investigation is reported of the rates of absorption and urinary excretion of "sulfaphenazol" ("orisul", N¹-(1-phenyl-5-pyrazolyl)-sulphanilamide), sulphamethoxypyridazine, and "sulfoxazole" (sulphafurazole). At weekly intervals each of 9 patients received by mouth 2 g. of either sulfaphenazol, sulphamethoxypyridazine, or sulphafurazole, the plasma and urine levels of free and total sulphonamide being estimated by the method of Bratton and Marshall. The plasma levels for sulfaphenazol were intermediate between those for sulphafurazole and sulphamethoxypyridazine and remained above 10 mg. per 100 ml. for at least 24 hours; some 12 to 16% of the drug was conjugated. About 21% of the dose was excreted in the urine within 8 hours, about 30% of the drug being conjugated. Free and conjugated sulfaphenazol have the same solubility [value not given]. A further study in 38 patients showed that sulfaphenazol does not diffuse through uninfamed meninges into the cerebrospinal fluid. The renal clearance of sulfaphenazol was between 1.03 and 1.79 ml. per minute. None of the patients showed signs of toxicity. The optimum dosage of sulfaphenazol for clinical treatment is discussed.

J. E. Page

Infectious Diseases

641. **Clinical and Psychopathological Aspects of Q Fever.** (Клиника и психопатология лихорадки Q) V. N. ILVINA, A. S. POLETAEV, G. K. UŠAKOV, L. K. HOHLOV, Z. I. GALKINA, V. N. SALJAEV, and A. A. STOLJARČUK. *Журнал Невропатологии и Психиатрии* [Ž. *Neuropat. Psihiat.*] 59, 295-303, No. 3, 1959. 2 figs., 6 refs.

Cases of Q fever were first reported in the U.S.S.R. in 1947-8, but in Yaroslav province the disease was unknown until 1957, when an outbreak occurred during which a series of 85 cases (90% in males) were observed in hospital. The onset was sudden in 86% of cases, the temperature rising within 48 hours to 40° C. (104° F.) with headache in almost all cases, rigors in 89.4%, muscle pains in the lumbar region, calves, and neck in 89.4%, joint pains in 27%, and hyperhidrosis in 87%. The pyrexia, which tended to be irregular, lasted 4 to 10 days in 58.8% of cases, 11 to 20 days in 17.6%, 21 to 30 days in 20%, and longer in the remainder, falling by lysis in most cases, but by crisis in a few. Treatment with "synthomycin" (chloramphenicol) and "biomycin" (aureomycin) usually resulted in rapid abatement of the fever. Bradycardia was observed in 40% of cases and tachycardia out of proportion to the temperature in 2.4%, while the blood pressure was reduced in the majority, including hypertensive subjects. There were no respiratory or gastro-intestinal symptoms apart from mild catarrhal changes and anorexia. Hepatomegaly was observed in 42.5% and splenomegaly in 22.3% of cases. The erythrocyte sedimentation rate was markedly increased in only about 20% of cases and leucocytosis occurred at the height of the disease in only 12.8%, leucopenia being observed in 60%, with a shift to the right and a relative lymphocytosis. Relapse occurred 1 to 10 days after the abatement of the pyrexia in 12.8% of cases, 2 patients relapsing twice. There were no fatal cases. The complement-fixation reaction with *Rickettsia burneti* antigen was positive (titre 1:160 to 1:480) in 59.2%.

Some form of neuropsychiatric disturbance was observed in 83 of the 85 cases. One patient developed a psychotic illness, with disorientation in time and space, excitation, euphoria, and later apathy and amnesia, which necessitated his temporary transfer to a mental hospital. Other neuropsychiatric manifestations included euphoria (more rarely apathy and melancholia) in the early stages, followed in the pyrexial period by psycho-sensory disturbances, hyperalgesia, adynamia, depression, feelings of unreality, depersonalization, oculo-vestibular disturbances, paraesthesiae, frank hallucinations (19 cases), pseudohallucinations (12 cases), and disturbance of sleep (62 cases). The facial expression was usually gloomy, with hypomobile facies and fixed gaze, and all the patients complained of extreme weakness and hypobulia. Intellectual processes were interfered with and the train of thought was frequently interrupted. The

clinical signs included exaggerated tendon reflexes, tremor of the outstretched fingers, tongue, and lips, and dermographia. In general, the neuropsychiatric state returned to normal with the temperature, but asthenia, adynamia, apathy, and hypobulia persisted for some time. It is pointed out that in view of the possible occurrence of severe "Q-fever psychoses" the rickettsioses should be used with great caution for pyrotherapy in psychiatry.

The results of biochemical investigations indicated a depression of enzyme formation in the liver and of the cholinesterase system.

S. W. Waydenfeld

VIRUS DISEASES

642. **Some Clinical Peculiarities of Tick-borne Encephalitis.** (Некоторые особенности клиники клещевого энцефалита)

V. A. FEDOROVA. *Журнал Невропатологии и Психиатрии* [Ž. *Neuropat. Psihiat.*] 59, 321-323, No. 3, 1959. 15 refs.

An account is given of 30 cases of tick-borne encephalitis with some unusual features which were observed during May and June, 1957. All the patients (19 men and 11 women) had been exposed to risk in the forest and all but 8 gave a definite history of tick bites. The polioencephalomyelitic and encephalitic forms of the disease were conspicuous by their absence. The meningeal form was diagnosed in 13 cases and the abortive form in 9; in the remaining 8 cases the condition was biphasic.

The incubation period was 2 to 4 days in 8 cases, in contrast to the usually accepted period of 7 to 8 days. The onset was usually acute, with pyrexia, headache, and vomiting, a prodromal period being observed in 5 cases only. The pyrexial period lasted 2 to 18 days. Contrary to general experience the erythrocyte sedimentation rate was increased in only 4 cases and the leucocyte count in none, a relative lymphocytosis being present in 12 cases. Meningeal signs were observed in 21 cases. The cerebrospinal fluid contained over 150 cells per c.mm. in 14 cases (400 to 650 per c.mm. in some), and there was evidence of dissociation between the cell count and protein content in 20 cases. Tenderness of the muscles of the neck and of the cervical vertebrae was an almost constant finding. Other findings included central facial paresis (6 cases), tenderness over the points of emergence of the branches of the trigeminal nerve (7), disturbances of vestibular function (14), oculomotor disturbance with nystagmoid reaction (6), diminution of the abdominal, knee, and ankle reflexes (8), and depression of deep muscle sense in the legs (7). All those manifestations were transient.

The biphasic form of the disease observed in 8 cases was considered to be nosologically identical with the

other forms of tick-borne encephalitis. The first, pyrexial, phase, usually of the abortive type, lasted 2 to 7 days and was followed after an interval of 2 to 17 days by the second phase, usually meningeal in type. This biphasic course was not seen in cases treated initially with intramuscular injections of specific antiserum (20 ml. on 3 successive days), but was observed in 4 cases in which mepacrine had been given during the first phase.

S. W. Waydenfeld

643. The Encephalitic Forms of Poliomyelitis. (Les formes encéphalitiques de la maladie de Heine et Médin)

S. THIEFFRY, C. MARTIN, and M. ARTHUIS. *Semaine des hôpitaux de Paris* [Sem. Hôp. Paris] 35, 1349-1355, April 18, 1959. 28 refs.

The authors describe 9 cases of poliomyelitis of encephalitic type which occurred at the Hôpital des Enfants-Malades, Paris, between 1956 and 1958 and review them in the light of Médin's original observations on this complication, made in 1898. According to the clinical picture presented the cases were divided into two groups: (1) those with Médin's original "ataxic form of poliomyelitis"; and (2) those with what the authors term "encephalitic forms" accompanied by tonic contractures, clonus, Parkinsonism, or convulsions.

The 5 patients in Group 1 were all males, aged 2, 2½, 4, 9, and 13 years respectively. The signs consisted in abnormal choreiform movements, oscillations of the eyeball, and clonus. All recovered in less than one month without any sequelae. Type-1 virus was isolated in 4 cases and Type 3 in one. Neutralizing antibodies to Type 1 were demonstrated in 2 of the former and to all 3 types in the latter case.

The 4 patients in Group 2 were all girls, aged 18 months and 9, 10, and 15 years respectively. The signs included coma or somnolence, paralysis, hallucinations, clonic and tonic movements, and Parkinsonism. The girls aged 9 and 10 years died, the diagnosis being confirmed at necropsy. The other two recovered, the only sequelae being peripheral palsies typical of poliomyelitis. Type-1 virus was isolated and the corresponding neutralizing antibody demonstrated in one of the latter cases and Type-2 virus was isolated in the other, but in the 2 fatal cases the diagnosis rested entirely on the necropsy findings.

I. M. Librach

644. The Contribution of Laboratory Examinations to the Diagnosis of Poliomyelitis. (Apport des examens de laboratoire pour le diagnostic de la poliomyélite)

S. THIEFFRY, M. ARTHUIS, C. MARTIN, J. CELERS, and V. DROUHET. *Semaine des hôpitaux de Paris* [Sem. Hôp. Paris] 35, 1343-1349, April 18, 1959. 11 refs.

The authors describe the laboratory findings in 311 cases of poliomyelitis admitted during the period 1954-7 to the Hôpital des Enfants-Malades, Paris, in which the clinical diagnosis was regarded as certain. There were 299 paralytic and 12 non-paralytic cases. In 288 of the 311 cases the virus was recovered from the stools. Of the 23 specimens giving negative results, 18 were

taken 10 days to 3 months after the clinical diagnosis had been made. Type-1 virus was recovered in 202 paralytic and 9 non-paralytic cases, Type 2 in 47 paralytic cases only, and Type 3 in 27 paralytic and 2 non-paralytic cases.

It is concluded that the chance of isolating the virus from the stools is nearly 100% before the 10th day of illness, after which it diminishes. Neutralizing antibodies are also present in the serum during the early days of illness, but the titre varies. These findings together constitute the most conclusive proof of the diagnosis, while their absence in an otherwise typical case militates against it. However, the presence of virus in the stools or of antibody in the blood does not necessarily imply that a case is actually one of poliomyelitis. Search for the virus is not necessary for the diagnosis of the ordinary form of poliomyelitis, but may be of interest in showing that the virus is capable of causing other neurological syndromes and aseptic meningitis.

I. M. Librach

645. Haemorrhagic Fever in the Nekouzskii Region. (Геморрагическая лихорадка в Некоузском районе) R. N. VASILBEVA. *Клиническая Медицина* [Klin. Med. (Mosk.)] 37, 57-61, March, 1959.

Many severe cases of acute haemorrhagic fever, including the Far-Eastern haemorrhagic nephroso-nephritis, have been reported from different parts of the Soviet Union in the last 20 years. The fever is endemic in certain areas, especially damp shrublands. A study of the type prevailing in the Nekouzskii region (Yaroslav province) showed that the disease is due to a filterable virus which is recoverable from the blood and urine of patients during the pyrexial stage. Infected serum can be neutralized by the serum of persons who have had the disease. The virus cannot be recovered from the secretions of the respiratory tract. The chief mode of spread seems to be by fomites infected with excreta of the field mouse, which is a carrier of the virus. Between October, 1953, and December, 1957, 460 cases (13 fatal) were diagnosed, the greatest incidence being in November, December, and January. Clinically, three stages of the illness, which has no prodromal period, can be distinguished. (1) The toxic stage, lasting for one to 5 days, accompanied by high fever, central abdominal pain, persistent vomiting, hiccup, backache, and asthenia. (2) The stage of haemorrhagic manifestations of varying intensity and of renal insufficiency, during which there appear erythema of cyanotic tinge, conjunctivitis, yellow discoloration of the sclera, mucosal haemorrhages, oedema of the face, a swollen, dry, and coated tongue, inflamed gums, halitosis, petechial haemorrhages and ecchymoses, excessive thirst, vomiting, hiccup, and a sustained high temperature, with lysis between the 4th and 9th days. Renal failure occurs in 96.8% of cases and is responsible for most of the deaths. Oliguria is often observed on the 4th or 5th day and may result in anuria and uraemia. (3) The stage of recovery; convalescence is slow and is accompanied by leucocytosis (up to 20,000 cells per c.mm.) and polyuria.

In this series the complications included pneumonia (6 cases), anuria (2), furunculosis (2), cerebral hae-

morrhage (3), meningoencephalitis (4), and thrombophlebitis, parotitis, and auditory neuritis (one case each). The 13 deaths were due variously to shock, uraemic coma, rupture of the renal cortex, cerebral haemorrhage, and renal apoplexy. Post-mortem findings included renal congestion and haemorrhages, oedema of the perirenal areolar tissue, and congestion of and haemorrhages in the intestinal mucous membrane, brain, and even muscles.

Treatment included the prophylactic administration of penicillin, calcium chloride, intravenous infusions of sodium chloride, glucose, and vitamins K, B₁, and C, and sometimes injections of camphor, nikethamide, strophanthin, or strychnine. In the haemorrhagic cases blood and plasma transfusions were given. A salt-free diet had no apparent beneficial effect. A rodent-extermination campaign was the main preventive measure adopted and has greatly reduced the incidence of the disease.

S. W. Waydenfeld

646. **Neuropsychiatric Disturbances in Influenza.** (Клинике психических расстройств при гриппе)
V. I. MAKSIMENKO. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] 59, 275-279, No. 3, 1959.

Certain neuropsychiatric complications of epidemic influenza, as seen in a series of 34 patients (22 males, 12 females) aged 17 to 55 years in whom the diagnosis was based on epidemiological, clinical, and in some cases virological and serological grounds, are described. The cases fell into three groups. The first consisted of 13 cases of influenzal psychosis with a favourable course, 2 to 8 weeks in duration. The clinical picture included amnesia, clouding of consciousness, ideas of persecution, and feelings of guilt. In some cases a depressive state led to catatonic stupor. Recovery was associated with amnesia for the acute stage of the disease and short-lived asthenia. Treatment was with general supportive measures, antibiotics, and "aminazine" (chlorpromazine).

In the second group (11 cases) the influenza was acute in onset, with severe and generalized symptoms and such complications as tonsillitis, bronchopneumonia, and haemorrhagic enteritis. The neuropsychiatric manifestations persisted for 3 to 8 months and included pyramidal disturbances, hemiplegia, facial paresis, vegetative disturbances, clouded consciousness, amentia with motor excitement, occasional visual and auditory hallucinations and delirium, suicidal tendencies, and accesses of unmotivated fear. The cerebrospinal fluid (C.S.F.) was under increased pressure, but was otherwise normal. In some cases hypertensive crises developed, with drowsiness, giddiness, hypotonia, sweating, pallor, cardiac arrhythmia, headache, psycho-sensory disturbances, and unilateral pyramidal signs. (In the author's opinion this syndrome of influenzal psychosis with hypertensive crises, characterized by catatonic and paranoid features and hypochondriacal complaints, is insufficiently recognized. The clinical picture differs from that of schizophrenia in the absence of prolonged disturbances of consciousness and subsequent personality changes.)

Treatment included dehydration therapy and cardiac supportive and general anti-infective measures.

The third group consisted of 10 cases of encephalitis. The clinical picture was one of toxæmia; the urine contained albumin and hyaline and granular casts and the blood non-protein nitrogen content was increased; there was leucocytosis with a shift to the left, a high erythrocyte sedimentation rate, and prolonged prothrombin time. The neuropsychiatric manifestations included both meningeal and focal symptoms, the latter including hemiplegia, hemiparesis, abnormal reflexes, and dysfunction of the pelvic organs. In unfavourable cases a hypertensive syndrome developed, with increased intrathecal pressure and an increased protein concentration and slightly increased cell count in the C.S.F. Amentia with psychomotor overaction was followed by apathy, and the state of consciousness oscillated between agitation and drowsiness and coma. Extrapyramidal manifestations were met with in 3 cases. Treatment was with antibiotic, antitoxic, and dehydration therapy. Four of the 10 patients died 8 to 14 days after onset, the necropsy findings being those of toxic and haemorrhagic encephalitis. Recovery in the remaining 6 cases was very slow.

S. W. Waydenfeld

647. **Clinicopathologic Study of Thirty-three Fatal Cases of Asian Influenza**

R. OSEASOHN, L. ADELSON, and M. KAJI. *New England Journal of Medicine* [*New Engl. J. Med.*] 260, 509-518, March 12, 1959. 7 figs., 16 refs.

The authors report from Western Reserve University School of Medicine, Cleveland, Ohio, that during the epidemic of Asian influenza in the autumn of 1957 33 sudden unexplained deaths occurred in and around Cleveland, 27 of these being investigated by the coroner. In these patients, of whom 19 were under the age of 40, the typical findings were an abrupt onset, constitutional and respiratory symptoms (which were frequently associated with similar illnesses in the family circle), characteristic pathological appearances, and the isolation at necropsy of the Asian strain of influenza virus in the majority of cases.

The respiratory clinical picture was of fulminant disease in the majority and encephalopathy in 4 cases (with normal ante-mortem lumbar-puncture findings in 2 of these). Death occurred within one week in 28 of the 33 cases. The pathological changes were those of a haemorrhagic, oedematous bronchopneumonia, and in 12 cases an eosinophilic hyaline membrane outlined the alveolar spaces. Tenacious, bloody, mucopurulent fluid frequently filled the lumen of the bronchi and bronchioles, and in the majority there was florid necrosis and confluent ulceration of the bronchial mucosa. Myocarditis was noted in one-third of the patients, and cerebral congestion, with a cerebellar pressure cone, in several. The brains of the 4 patients with encephalopathy were free of inflammation. Influenza virus was isolated from the respiratory tract of 25 patients, and from other tissues (liver, spleen, kidney, heart, lymph nodes, and tonsil) of 3. Haemolytic staphylococci were isolated from the respiratory tract in 13 cases and pneu-

mococci in 7, but the type and severity of the inflammation were independent of the presence or absence of bacteria. It is concluded that the findings in this study lend support to "the concept of viremia in overwhelming influenza infection in man". *D. Geraint James*

648. Clinical Features of Infection with Haemadsorption Viruses

R. H. PARROTT, A. VARGOSKO, A. LUCKEY, HYUN WHA KIM, C. CUMMING, and R. CHANOCK. *New England Journal of Medicine* [New Engl. J. Med.] 260, 731-738, April 9, 1959. 2 figs., 4 refs.

The isolation of two new myxoviruses, haemadsorption virus Types 1 and 2, was reported by Chanock *et al.* in 1958 (*New Engl. J. Med.*, 258, 207). In this paper the clinical features in children with infection due to these viruses are reported. These myxoviruses have the properties of haemadsorption on tissue culture and haemagglutination of chicken and guinea-pig erythrocytes. A complement-fixing antigen is available and it is possible to estimate antibodies quantitatively.

In the winter of 1957 and the spring of 1958 these specific haemadsorption viruses, Types 1 and 2, were isolated from 6% of 879 children with respiratory-tract infection, in hospitals in the area of Washington, D.C. Clinical details were available in respect of 42 children infected with Type-1 haemadsorption virus and 50 infected with Type-2 haemadsorption virus. There were few clinical differences between the two types of infection and no specific syndromes which could be related to these organisms. The symptoms and signs observed are common to a number of different infections—that is, cough, coryza, and sore throat. In a small proportion (9%) who were more severely ill the main clinical features were those of a lower respiratory or pneumonic infection.

The authors state that without the aid of laboratory tests it is impossible to reach a specific diagnosis of this infection.

John Fry

BACTERIAL DISEASES

649. Kanamycin in Bacillary Dysentery

K. FUKAYA, M. SUZUKI, S. ISHII, A. KAWASHIMA, K. ENOMOTO, H. TAKAYAMA, and O. KITAMOTO. *Japanese Journal of Experimental Medicine* [Jap. J. exp. Med.] 29, 37-43, Feb. [received May], 1959. 5 refs.

Kanamycin, an antibiotic derived from *Streptomyces kanamyceticus*, an organism isolated from Japanese soil, has hitherto been known as a useful agent in streptomycin-resistant tuberculosis. Its antibacterial spectrum resembles that of streptomycin. In this paper from the Hospital of the Institute for Infectious Diseases, University of Tokyo, a study is reported of the efficacy of this antibiotic in *Shigella* infections.

Kanamycin was given by mouth to 48 patients suffering from dysentery due to *Shigella flexneri*, Types 2a, 2b, and 3a, in a dosage of 60 mg. per kg. body weight 4 times a day. [This somewhat high dosage was apparently

based on the results of sensitivity tests *in vitro* in which these strains were sensitive to the drug at an average minimum inhibiting concentration of 7.1 μ g. per ml.] The clinical and bacteriological results were favourable in all cases; bacteriological relapse occurred in 2 cases only. Intramuscular injection in 6 cases was less effective than oral administration. A combination of kanamycin and chloramphenicol was also effective in the 7 cases in which this was tried. The serum agglutination titres against *Sh. flexneri* 2a, 2b, and 3a and *Sh. sonnei* were determined before treatment started; there was no fall after administration of kanamycin, an increase being observed in some cases.

It is concluded that the action of kanamycin in shigellosis is similar to that of other broad-spectrum antibiotics, and that it may be particularly useful in cases which are resistant to these. The authors state that the only disadvantage of this treatment is a tendency to loose stools for some time afterwards, this probably being associated with the virtual disappearance of *Escherichia coli* and some other organisms from the stools, with occasional appearance of *Streptococcus faecalis*, *Proteus*, and *Candida*.

H. Stanley Banks

650. Blood Transfusion in the Prevention of Relapses of Typhoid and Paratyphoid Fevers. (Гемотрансфузии в профилактике рецидивов тифо-паратифозных заболеваний)

Z. A. КОМОВА. *Клиническая Медицина* [Klin. Med. (Mosk.)] 37, 49-52, March, 1959. 11 refs.

The author reports that although preventive measures have greatly diminished the incidence of typhoid and paratyphoid fevers and "synthomycin" (chloramphenicol) and "biomycin" (aureomycin) treatment have similarly reduced morbidity and mortality, nevertheless the relapse rate has increased. Thus relapses were observed in 40 (12.7%) of 314 patients treated symptomatically and in 84 (26.3%) of 319 patients treated with synthomycin in addition. Most of the relapses were mild and easily controlled by another course of antibiotics, but 21 patients relapsed twice and 4 patients three times, each relapse requiring a further 3 weeks' isolation. As a result the average period of isolation in 1957 was 30 days compared with 26.2 days in 1949 before synthomycin was in general use.

Of 36 patients treated with synthomycin the opsonin-phagocytic index of the blood, compared with its value before treatment, was increased in one, unchanged in 6, and reduced in 29. The titre of agglutination reaction with Strain Ty-2 was increased in 2, unchanged in 8, and diminished in 7 cases, while in a further 19 cases the reaction became negative. In order to counteract the depression of immunological response caused by the synthomycin, and so to diminish the incidence of relapse, blood transfusion was given (in addition to synthomycin) to 63 patients with typhoid and 2 patients with paratyphoid-B fever. The 50 adults so treated were given 100 ml. of blood and the 15 children 50 to 60 ml. at each transfusion, 7 patients receiving 3 to 5 transfusions, 24 two transfusions, and 34 one transfusion, with an interval between transfusions of 4 days. Relapse occurred

in only 8 of these 65 patients, the incidence being thus reduced to the level observed in the symptomatically treated cases. The opsonin-phagocytic activity, as determined in 14 of the patients given combined synthomycin-transfusion treatment, was increased in 11 cases, unchanged in one, and diminished in only 2. It is stressed that the transfusion of whole blood is necessary, since the transfusion of plasma only does not diminish the incidence of relapse. S. W. Waydenfeld

651. Brucellosis. I. Laboratory-acquired Acute Infection

R. W. TREVER, L. E. CLUFF, R. N. PEELER, and I. L. BENNET. *A.M.A. Archives of Internal Medicine* [A.M.A. Arch. intern. Med.] 103, 381-397, March, 1959. 10 figs., 23 refs.

From 1945 to 1957 60 cases of acute brucellosis occurred among personnel of a bacteriology laboratory at the Johns Hopkins University School of Medicine, Baltimore, who were engaged in studies of *Brucella melitensis* and *Br. suis*. The majority of the patients were white males aged 20 to 40 years. The diagnosis was made by isolation of *Brucella* from the blood or marrow aspirate of the acutely ill patient, by observation of a rise in the serum agglutinin titre to 1:100 or greater, or by both methods. Serological studies before, during, and after the infection showed that the agglutinin titre rises uniformly very early in the course of the infection and the agglutination reaction is almost invariably positive when the patient becomes acutely ill. A laboratory accident was known to have occurred in 21 cases, and in these the interval between the accident and the appearance of symptoms of brucellosis averaged 6 weeks.

The mode of onset varied considerably: the most prominent symptoms, occurring in one-half of a group of 22 patients, were malaise and fatigue. The maximum temperature recorded varied; 8 of the 60 patients were afebrile, while in 5 cases the temperature rose as high as 105° to 106° F. (40.6 to 41.1° C.). In none of the 8 patients who were afebrile was the blood culture positive, whereas 7 of 8 who had an undulating fever were bacteraemic. Salicylates were given intermittently to 34 patients, 12 of whom developed rigors soon after taking the drug. The complications observed included epididymitis, swelling of the testis or breast, synovitis, and malleolar ulcers; other disease processes associated with acute brucellosis were not common. In 12 cases no specific treatment was given; in the other cases treatment included the administration of tetracycline or streptomycin or both; the only apparent result of antibiotic treatment was a more rapid disappearance of the bacteraemia while the drugs were being given.

Among the more interesting observations made in this series were: coexistent pneumococcal pneumonia (in one case); symmetrical ulcers of the ankles due to *Br. suis*; development at different times of tularaemia and brucellosis in the same patient; and a Herxheimer reaction associated with recurrent bacteraemia apparently related to streptomycin and tetracycline therapy. A diagnosis of "chronic brucellosis" was made in 24

cases in which the patient complained of malaise, fatigue, myalgia, arthralgia, backache, or feverishness for a period of one year or more after the acute illness, these symptoms not being associated with bacteraemia, with changing serological titre, or with abnormal physical signs.

R. G. Meyer

652. Brucellosis. II. Medical Aspects of Delayed Convalescence

L. E. CLUFF, R. W. TREVER, J. B. IMBODEN, and A. CANTER. *A.M.A. Archives of Internal Medicine* [A.M.A. Arch. intern. Med.] 103, 398-405, March, 1959. 6 refs.

A follow-up study was made at the Johns Hopkins University School of Medicine, Baltimore, of 24 of the 60 patients who had acquired acute brucellosis, due to infection with *Brucella suis* or *Br. melitensis*, in the course of laboratory work 4 to 8 years previously [see Abstract 651]. The series comprised: (I) 10 patients who had been diagnosed as having "chronic brucellosis" and who were still symptomatic at the time of the study; (II) 6 patients who had been diagnosed as having "chronic brucellosis", but who were asymptomatic at the time of the study; and (III) 8 patients who had been well since their recovery from acute brucellosis. The symptoms which had led to the diagnosis of "chronic brucellosis" included depression, fatigue, sexual impotence, and vague aches and pains.

Careful clinical investigation failed to demonstrate any difference between the three groups apart from the continued symptoms in Group I, while the results of serological and other laboratory tests were also similar. A retrospective study showed that it was impossible to predict in which cases of acute infection chronic disability was likely to develop. All the patients investigated were hypersensitive to the antigens of *Brucella*, but there was no detectable difference in the degree of hypersensitivity to brucellergen between the three groups of patients and there was no evidence of persistence of *Brucella* infection. Minor abnormalities were present in the electroencephalogram in several cases, but these were as frequent in Groups II and III as in Group I.

The authors consider that the resemblance of the symptoms of "chronic brucellosis" to psychoneurosis suggests the possibility that psychological factors may be of importance in the pathogenesis of this disease.

R. G. Meyer

653. Brucellosis. III. Psychologic Aspects of Delayed Convalescence

J. B. IMBODEN, A. CANTER, L. E. CLUFF, and R. W. TREVER. *A.M.A. Archives of Internal Medicine* [A.M.A. Arch. intern. Med.] 103, 406-414, March, 1959. 8 refs.

A psychological investigation was carried out as part of the follow-up study [see Abstract 652] of 24 patients with a history of acute brucellosis 2 to 8 years previously. All but one of the patients were male, and the series included 2 negroes and one "oriental"; 9 of the patients were employed in semi-skilled or unskilled work and one of these was illiterate. The examination of the patients consisted of psychological testing and psychi-

atric interviews. The results of psychological tests evaluating certain areas of intellectual functioning did not demonstrate any significant differences between the patients with "chronic brucellosis" and those who had recovered uneventfully from the infection, but it was found that emotional disturbances, especially depression, were significantly more prevalent in the former. The results of the psychological tests and the biological data obtained from the psychiatric interviews suggested that these disturbances were not a consequence of the persisting symptoms of the disease. The authors therefore conclude that the emotional disturbances were more critically related to the pre-illness personality structure and the concurrent life situation, and they consider that emotional disturbance constitutes the essential component of "chronic brucellosis".

R. G. Meyer

INFECTIOUS DISEASES OF UNKNOWN AETIOLOGY

654. Benign Myalgic Encephalomyelitis. An Outbreak in a Nurses' School in Athens

G. K. DAIKOS, S. GARZONIS, A. PALEOLOGUE, G. A. BOUSVAROS, and N. PAPADOYANNAKIS. *Lancet* [Lancet] 1, 693-696, April 4, 1959. 2 figs., 13 refs.

An epidemic of acute myalgic encephalomyelitis occurred in June, 1958, and affected 27 nurses at the Queen Frederica School for Midwives (Alexandra Hospital), Athens; no patient or physician was affected. The prodromal symptoms were muscle pains which lasted 2 to 3 weeks and were accompanied by numbness and weakness of the lower limbs, headache, anorexia, malaise, and general symptoms of pyrexia. When the disease had fully developed the pains and weakness became more marked, and muscle contractions and subjective sensory changes were reported. These symptoms were very variable and fluctuated from day to day. Cranial nerve involvement was not observed, but a few of the patients complained of diplopia. There was extreme tenderness of the periosteum and periarticular tissues, and local swelling of the hand or foot occurred in 3 patients. There were numerous psychiatric disturbances, including emotional instability, depression, and sometimes euphoria and frank hysteria, but these disturbances were transient and did not require special treatment.

Laboratory investigations all gave negative results; electroencephalography in 4 patients gave a normal recording in 3, but showed abnormal slow activity in one severely affected patient. Electromyography revealed myopathic lesions in 4 out of 6 patients so tested. The duration of the disease was up to one month in half the patients, but some had repeated relapses. Although the results of bacteriological and viral studies were negative, such an origin was strongly suspected. Since only the nurses living closely together in the nurses' home were affected, it appeared that continuous and intimate contact coupled with an infective focus was necessary for infection. No form of therapy appeared to influence the course of the malady, but there were no deaths.

Winston Turner

655. Epidemic Myalgic Encephalomyelopathy. The Durban Outbreak

R. C. J. HILL, R. W. S. CHEETHAM, and H. L. WALLACE. *Lancet* [Lancet] 1, 689-693, April 4, 1959. 2 figs., 8 refs.

An epidemic is described which occurred with dramatic suddenness near the end of the summer (February) of 1955 and which affected 98 of the nursing staff of Addington Hospital, Durban, Natal, of whom 59 became ill within one week. Other members of the hospital staff (totalling 446) and patients were not affected, but further cases occurred later outside the hospital. The aetiology was obscure, but assuming the disease to be due to an infective agent the incubation period was 7 to 14 days. Children below the age of puberty were not affected and the greatest incidence occurred in those between the ages of 16 and 25. The clinical course could be divided into 4 distinct phases: prodromal, acute, convalescent, and chronic.

The patients presented with severe occipital headache and lassitude and the symptoms of an acute upper respiratory infection, accompanied by excessive sweating. This was followed by weakness or paralysis of the limbs, especially on the left side, with paraesthesiae and severe muscle pains and cramps. The convalescent period was variable, ranging from one to 3 months, and relapses were frequent. In 11 cases the disease entered the chronic phase, with persistent but variable degrees of paralysis or weakness lasting up to 3 years after the onset.

The physical signs and the results of pathological investigations are fully described; there were no grossly abnormal findings. Viral, bacteriological, and toxicological studies gave only negative results. Muscle biopsy examination and electrophysiological tests revealed no abnormal findings. The psychological changes were the most important and included euphoria, depression, lack of concentration, emotional instability, and other personality changes [but it is not stated how long these disturbances persisted]. The authors describe some similar epidemics which have been reported from other areas, and conclude that the disease described was a myalgic encephalomyelopathy.

Winston Turner

656. A Myopathy of Boeck's Sarcoid

J. C. HARVEY. *American Journal of Medicine* [Amer. J. Med.] 26, 356-363, March, 1959. 5 figs., 23 refs.

Cases of Boeck's sarcoid with involvement of the skeletal musculature alone are very rare. At Johns Hopkins Hospital, Baltimore, bilateral symmetrical muscle-wasting, affecting principally the shoulder and pelvic-girdle muscles, has been observed in 3 adults over the last 15 years. Examination of biopsy specimens of the pectoral, biceps, or gastrocnemius muscles revealed a sarcoid-tissue reaction. None of the patients showed evidence of generalized sarcoidosis on clinical or radiological examination or in biopsy specimens from lymph nodes and skin. These localized sarcoid-tissue reactions in skeletal muscle were accompanied by recurrent fever, arthralgia, and myalgia with associated weakness. Steroid therapy appeared to arrest the progress of the myopathy.

D. Geraint James

Tuberculosis

657. Towards the Total Elimination of Tuberculosis. (На пути ликвидации туберкулеза)

I. D. ZASLAVSKIY. *Клиническая Медицина* [Klin. Med. (Mosk.)] 37, 3-8, March, 1959.

During the period 1949-55 the incidence of tuberculosis in the towns of the Soviet Union was reduced by 43%, the percentage reduction being relatively greater among children and adolescents and also in the more destructive forms of the disease. Thus the incidence of fibro-caseous tuberculosis has been reduced 5-fold and of neglected forms of pulmonary tuberculosis 4-fold, while miliary tuberculosis, tuberculous meningitis, and caseous pneumonia have become rare. Similarly the over-all mortality from tuberculosis has been reduced 3-4-fold, mainly in the younger age groups. In 1939 tuberculosis was responsible for 22.5% of all male deaths and 34% of all female deaths below the age of 19, whereas in 1956 the corresponding figures were 1.5 and 3.5%. At the same time, however, there has been a relative increase in the mortality from tuberculosis in persons aged over 60. The main factors responsible for this improvement are better living and working standards, together with the development of special anti-tuberculosis services. These have included (1) immunization of all newborn babies and subsequent periodical re-immunization; (2) mass radiographic and clinical examination of the population with the aim of diagnosing the disease in its early stages; (3) the widespread use of specific antituberculous drugs in combination with older methods of treatment.

The author states that complete eradication of tuberculosis within the next 15 to 20 years is considered a practical possibility. The plan for 1959-65 includes: (1) Sanitary measures aiming at increased "herd resistance", with popularization of physical culture and education in prevention. (2) Inoculation of all non-infected children, adolescents, students of higher and medium grade educational establishments, and employees in the health services up to 30 years of age. (3) An increase in the number of mobile mass x-ray units so as to provide one unit per 300,000 of the population, thus allowing each person to be examined every 2 or 3 years. (4) Introduction of the Pirquet test for all children over 3 months; in those giving a negative reaction the test will be repeated twice a year until the age of 4 and once a year thereafter. (5) All clinics, hospitals, and sanatoria having over 150 beds to be equipped to carry out tomography and bronchoscopy, and all district and regional hospitals of the 1st and 2nd categories to be provided with microbiological laboratories. (6) The organization of long courses of free treatment (lasting 6 to 12 months or even more) with antituberculous drugs at out-patient departments or in the patient's home, such treatment being maintained for up to 12 months in the case of early disease in children and adolescents and for 4 to 8 months in adults, for 2 to 4 months in patients with

exacerbation of chronic disease, and for 1 to 2 months in case of compensated chronic lesions. (7) Occupational therapy and rehabilitation departments to be set up in all large sanatoria and hospitals (over 150 beds); by 1965 there should be 2 beds per 1,000 of the population reserved for the treatment of tuberculosis. (8) Lastly, intensification of scientific research into all problems connected with tuberculosis.

In view of the connexion between the disease and aspects of the patient's life not under the control of the health authorities it is recommended that special antituberculosis committees be organized within the local councils, such committees to include representatives of collective farms, state farms, industrial establishments, health services, educational authorities, social insurance authorities, and the trade unions.

S. W. Waydenfeld

658. Reversal of Tuberculin Reaction in Early Tuberculosis

J. M. ADAMS, V. A. KALAJAN, B. O. MORK, M. ROSENBLATT, W. J. ROTHROCK, and B. J. O'LOUGHLIN. *Diseases of the Chest* [Dis. Chest] 35, 348-356, April, 1959. 1 fig., 10 refs.

From the University of California the authors report an investigation into the significance of reversal of the tuberculin reaction carried out at tuberculosis clinics in the city and county of Los Angeles, in which 121 out of 160 subjects of all ages, half of them under 6 years of age, previously known to have been negative tuberculin reactors, were followed up by repeated skin tests after it was found that the reaction had become positive. In 68 (56%) of these the reaction subsequently reverted from positive to negative, including 17 out of 28 infants aged less than one year, 40 out of 69 (58%) who had converted from negative to positive within 3 months, and 11 out of 24 (46%) who had converted within 12 months. It was also demonstrated that the percentage of those reverting was inversely correlated with the size of the skin reaction (6 to 10 mm. 76%; 11 to 20 mm. 50%; and over 20 mm. 38%). These findings, the authors suggest, may indicate that repeated testing provides a means of detecting early tuberculous disease.

In a series of animal experiments they showed that skin reactivity was diminished in guinea-pigs treated with isoniazid compared with that in untreated controls. Animals in which treatment coincided with skin testing failed to develop a positive reaction, while those in which treatment followed inoculation showed only weak reactions. They point out that the mechanism governing these phenomena may not be the same in man as in the guinea-pig. Among the patients tested a change in the tuberculin reaction from positive to negative was most frequent in individuals in whom the chest radiograph was normal, and such change did not occur in those in whom radiography revealed evidence of active tubercu-

lous disease. The authors conclude with a plea for repeated tuberculin skin testing of known positive reactors.

Raymond Parkes

659. Medical Treatment as an Alternative to Thoracoplasty in Pulmonary Tuberculosis

P. G. ARBLASTER, I. R. MCWHINNEY, R. A. SMITH, and K. W. CROSS. *Thorax* [Thorax] 14, 14-20, March, 1959.

This investigation was designed to determine the results of treatment of pulmonary tuberculosis in a group of patients considered suitable for thoracoplasty but on whom no operation was performed. Of 1,183 cases of tuberculosis notified in South Warwickshire between 1946 and 1955, 259 were selected as suitable for thoracoplasty. Operation was performed in 72 of these; the remaining 187 medically treated cases were divided into two groups—94 treated before and 93 treated after 1952, when effective antibacterial drugs were available.

Of these 187 patients, 53% were away from work more than 8 months, those under 30 years of age being away the longest periods. Of 68 patients with a positive sputum who were treated before 1952, 53 became sputum-negative; of 62 similar patients treated after 1952, only one failed to show sputum conversion. At the conclusion of the investigation it was found that 45 (66%) of the former group were fit for full-time work compared with 51 (82%) of the latter group. Radiological examination revealed that of the 94 patients treated before 1952, 56 improved and 16 became worse, the figures for the group of 93 treated after 1952 being 69 and 2 respectively. The efficacy of adequate chemotherapy was most marked in the age group 30 to 44 years.

There was a relapse in 36 cases in the series, in 15 of which misinterpretation of radiographs or "inadequate use of available antibacterial drugs" was considered to be an important factor. Of the 9 patients who died, only one was treated after 1952, and death in this case was due to progressive muscular atrophy, not tuberculosis.

L. Capper

660. The Diagnosis of Tuberculous Pleural Effusion

P. MESTITZ and A. C. POLLARD. *British Journal of Diseases of the Chest* [Brit. J. Dis. Chest] 53, 86-94, Jan., 1959. 1 fig., bibliography.

The value of a number of indirect aids in the diagnosis of tuberculous pleural effusion was studied at the Middlesex Hospital, London, in 112 patients with pleural effusion of proven aetiology. In 73 of the patients the effusion was tuberculous, and the ages of this group ranged from 17 to 51 years. The onset was usually insidious, but might be sudden; the size of the effusion was of no help in diagnosis. The reaction to the Mantoux test was positive in all of the 66 cases in which the test was performed. The erythrocyte sedimentation rate (E.S.R.) varied between 11 and 118 mm. in one hour, a range similar to that found in 27 patients with malignant disease. The pleural fluid was never frankly purulent, but in one case it was blood-stained. Cytological examination of the fluid in 68 cases revealed "almost pure blood" in one case and "mainly endothelial cells" in one. In 65 of the remaining 66 cases,

however, lymphocytes were predominant, and in those cases in which a formal differential count was carried out the percentage of lymphocytes was always more than 72 and usually more than 85. Only in one case of proved tuberculous pleural effusion did polymorphonuclear leucocytes predominate. Tubercle bacilli were found on direct examination in only one out of 40 cases. Culture of pleural fluid, with or without guinea-pig inoculation, was positive for tubercle bacilli in 24 of the 73 cases, whereas the results of pleural biopsy were positive in 70.

The authors consider that pleural biopsy is by far the most certain aid in the diagnosis of a tuberculous effusion, other helpful procedures being examination of the cytology and bacteriology of the pleural fluid and the tuberculin skin test. They state that an effusion is unlikely to prove tuberculous unless the reaction to the tuberculin skin test is positive and the pleural fluid is predominantly lymphocytic. Pleural biopsy, although usually giving positive results, may sometimes fail, as in 3 cases in the present series.

Arthur Willcox

661. Prednisone in the Treatment of Tuberculous Pleural Effusions

S. S. PALEY, J. P. MIHALY, E. L. MAIS, S. A. GITTENS, and B. LUPINI. *American Review of Tuberculosis and Pulmonary Diseases* [Amer. Rev. Tuberc.] 79, 307-314, March, 1959. 6 figs., 49 refs.

After a short discussion of the advantages and disadvantages of corticosteroids in the treatment of tuberculous pleural effusion the authors report their own experience with prednisone in 26 cases at Harlem Hospital, New York. It was thought that the anti-inflammatory properties of the steroid would be of particular benefit, notably in preventing the formation of organized pleural exudate.

On diagnosis thoracocentesis was performed and as much fluid as possible removed from the pleural sac, the following treatment being then instituted: 1 g. of dihydrostreptomycin three times weekly [the reason for choosing this form of streptomycin is not stated], together with 300 mg. of isoniazid daily, the intention being for this regimen to be continued for 2 years; simultaneously prednisone was given in a dosage of 30 mg. daily for 4 days, then 200 mg. daily for 7 to 14 days depending on response, and finally 10 mg. daily for the balance of the 4-week period; at the end of this course the majority of patients were given 25 units of corticotrophin. During the treatment partial bed rest was enforced for 2 to 3 weeks and then relaxed. In no case was intrapleural instillation of any drug employed. All 26 patients improved rapidly, and residual effusions (determined radiographically) resolved with unexpected speed in most. The average stay in hospital was 8 weeks (range 3 to 12 weeks). The radiological appearances returned to normal in 12 of the 26 patients, while only minimal abnormalities remained in the others. Significantly, no case of "disabling fibrothorax" was observed in a follow-up period of 18 months from the beginning of treatment.

Raymond Parkes

Venereal Diseases

662. Comparison between the Reactivity of Cardiolipin Antigen and a Lecithin-free Cardiolipin Antigen (Cardchol) in TPI-reactive and TPI-non-reactive Sera

H. SCHMIDT. *British Journal of Venereal Diseases* [Brit. J. vener. Dis.] 35, 47-52, March, 1959. 1 fig., 29 refs.

A comparison of two different cardiolipin antigens was carried out at the State Serum Institute, Copenhagen, on a total of 376 sera, 177 being reactive to the treponemal immobilization (T.P.I.) test and 199 non-reactive. Each serum was subjected simultaneously to two complement-fixation tests, one using "ordinary" cardiolipin antigen mixed in the proportions described by Maltaner and Maltaner (*J. Immunol.*, 1945, 51, 195) and the other using "cardchol", which is a mixture of cardiolipin and cholesterol in the same proportions as in ordinary cardiolipin antigen, but containing no lecithin.

It was found that with T.P.I.-reactive sera the reactivity of the ordinary cardiolipin antigen was superior to that of cardchol, whereas with about 50% of the non-reactive sera the reactivity of cardchol was superior to that of the ordinary cardiolipin antigen. It is concluded that the reactivity of cardchol to antilipoidal antibodies is greater when these are of a non-syphilitic nature.

R. R. Willcox

663. The Demonstration of a Common Antigen in Reiter's Treponeme and Virulent *Treponema pallidum*

G. R. CANNEFAX and W. GARSON. *Journal of Immunology* [J. Immunol.] 82, 198-200, March, 1959. 4 refs.

In experiments carried out at the University of North Carolina specimens of pooled human syphilitic serum were absorbed with V.D.R.L. slide-test antigen, with protein antigens prepared from the Reiter cultivable treponeme and from virulent *Treponema pallidum* by the method of D'Alessandro and Dardanoni (*Amer. J. Syph.*, 1953, 37, 137), and with the antigen used in the *T. pallidum* complement-fixation (T.P.C.F.) test of Portnoy and Magnuson. After incubation with the antigen each specimen was filtered and the filtrate subjected to the V.D.R.L. and T.P.C.F. tests and to complement-fixation tests with the two other antigens used for absorption, the results being compared with those of the same tests carried out on unabsorbed serum.

Absorption of the serum with V.D.R.L. antigen completely removed reactivity with this antigen, but left the titres in the other tests unaltered, showing that the treponemal antigens used react with substances distinct from the reagin present in syphilitic serum. Absorption with protein from virulent *T. pallidum* removed reactivity with this protein and with the protein prepared from the Reiter treponeme, but did not affect the titre of the T.P.C.F. or V.D.R.L. reaction. Absorption of the serum with protein from the Reiter treponeme abolished reactivity with this antigen, but left the titres of the other reactions unchanged. Rabbits injected

intravenously with Reiter protein antigen developed antibodies to this protein and, to a lower titre, to the protein from virulent *T. pallidum*, but their serum gave negative results with the V.D.R.L. and T.P.C.F. tests.

The authors conclude that the demonstration that the Reiter treponeme shares a common antigen with virulent *T. pallidum* strengthens the position of the Reiter protein complement-fixation test as a specific serological test for syphilis.

A. E. Wilkinson

664. Disease of the Heart and Aorta in 125 Treated Syphilitics. (Bilan cardio-aortique chez 125 syphilitiques)

L. VAN DER MEIREN, L. CRAPS, and J. LEQUIME. *Acta clinica Belgica* [Acta clin. belg.] 13, 521-530, Nov.-Dec., 1958 [received April, 1959]. 3 figs.

At the University Venereal Disease Clinic and the Hôpital Saint-Pierre, Brussels, the heart and aorta in 125 treated syphilitics were investigated clinically, radiologically, and electrocardiographically for the following reasons: (1) a clinical diagnosis of an aortic or cardiac lesion had been made at the beginning of treatment (9 cases); (2) manifestations of tertiary syphilis had been observed at other sites (18); (3) to determine why serological tests for latent syphilis remained positive after treatment (48); (4) to provide further data in cases of treated latent syphilis assumed to be cured. There were 46 male and 79 female patients.

A total of 24 patients (19.2%), 7 men and 17 women, including the 9 known cases were found to have a cardiac or aortic lesion of a specific nature; the average age of the men was 52 years and of the women 63. Of the 18 patients in Group 2 in whom tertiary lesions had been noted in other parts of the body aortitis was discovered in 4 (22.2%). Among the seroresistant patients with latent syphilis a cardiac or aortic lesion was found in 2 (11%) of the 18 males and 5 (16.6%) of the 30 females. Of the 50 cases of latent syphilis which were considered to be cured, cardio-aortic lesions were found in 3 women (6% of the group). The authors stress the importance of detailed examination of the cardiovascular system in all cases of syphilis, and point out that it is particularly in cases of seroresistant latent syphilis that periodic examinations have the greatest value.

R. D. Catterall

665. Ocular Lesions in 125 Treated Syphilitics. (Bilan oculaire chez 125 syphilitiques anciens)

L. VAN DER MEIREN, L. CRAPS, and L. COPPEZ. *Acta clinica Belgica* [Acta clin. belg.] 13, 531-540, Nov.-Dec., 1958 [received April, 1959]. 3 figs.

Examination of the eyes of the 125 treated syphilitics previously reported [see Abstract 664] showed that 21 (16.8%) had ocular lesions due to syphilis; (patients showing the Argyll Robertson pupil reaction only were not included). In 9 of these patients the ocular lesion had been present when treatment was

started; of 33 patients with tertiary syphilis the ocular involvement, present in 6 cases, was found only on examination by an ophthalmologist. Of a group of 36 patients with apparent latent syphilis, 6 were shown to have ocular lesions on ophthalmological examination, while of 47 patients whose serological tests had become negative following treatment, evidence of healed eye lesions was found in 2. The authors stress the value of detailed examination of the eyes in all cases of syphilis, and point out the value of healed lesions of the eyes in making a retrospective diagnosis. R. D. Catterall

NON-SPECIFIC URETHRITIS

666. PPLO of Human Genital Origin. Serological Classification of Strains and Antibody Distribution in Man

D. H. CARD. *British Journal of Venereal Diseases* [Brit. J. vener. Dis.] 35, 27-34, March, 1959. 22 refs.

Serological studies of strains of pleuropneumonia-like organisms (P.P.L.O.) isolated from cases of non-gonococcal urethritis (N.G.U.) and of sera from various groups of subjects were carried out at the Lister Institute of Preventive Medicine, London, as part of an investigation into the significance of P.P.L.O. in the aetiology of the disease. As agglutination tests are not practicable with P.P.L.O. a complement-fixation technique was used [the details of which should be obtained from the original paper]. Antisera were prepared against one strain of cattle pleuropneumonia organism and 6 human genital strains, human mouth and rat strains, and a saprophytic strain of P.P.L.O. and used in complement-fixation tests against various P.P.L.O. strains, including 56 of the 98 strains isolated by Klieneberger-Nobel (*Brit. med. J.*, 1959, 1, 19; *Abstr. Wld Med.*, 1959, 25, 402) from cases of N.G.U. and other genital infections in man. Cross-reactions occurred with all the strains and all the antisera, but the titre given by any strain with the homologous antiserum was usually significantly higher than that given with other antisera.

This survey showed that the human genital strains form a serological group distinct from the other P.P.L.O. strains, though they are not quite antigenically homogeneous among themselves. One of the strains tested (Strain 56) cross-reacted with 30 human genital strains to about the same titre as the homologous strain, suggesting that it contained an antigen common to these strains. An antigen made from Strain 56 was therefore used in the examination of human sera from a number of different sources for the presence of antibodies to human genital P.P.L.O. Positive reactions were obtained with 34.2% of 700 sera from patients attending two venereal disease (V.D.) clinics, 6.1% of 198 from medical out-patients, 6.3% of 96 from antenatal patients, 20.4% of 44 from gynaecological patients, 2.1% of 297 from blood donors, and 2% of 104 from children under 13 years of age. The incidence of P.P.L.O. antibodies in female V.D. patients (44.5%) was significantly higher than that in male V.D. patients (18.7%) ($P<0.01$) and that in gynaecological patients ($P=0.01$), which in turn

was significantly higher than the incidence in antenatal patients ($P<0.02$). It is especially noteworthy that there was no significant difference between the incidence in patients with N.G.U. and that in V.D.-clinic patients as a whole. In men with a history of syphilis or yaws the incidence of P.P.L.O. antibodies was significantly higher than the average for clinic patients, but a history of syphilis or yaws was also quite common among patients without P.P.L.O. antibodies and any antigenic overlap between the two conditions is considered to be of minor importance. The conditions may be concurrent—P.P.L.O. were demonstrated in the serous fluid from 2 syphilitic chancres. There was no significant correlation between the results of simultaneous serological and cultural tests for P.P.L.O. on 26 V.D.-clinic patients, 10 gynaecological patients, and 5 others.

The distribution of antibodies to P.P.L.O. found was in accordance with the expected incidence of V.D. in the groups tested and ran roughly parallel with the frequency of isolation of P.P.L.O. from the urogenital tract in various similar groups reported by Klieneberger-Nobel. However, it is not possible to draw conclusions from these findings about the exact role of P.P.L.O. in the causation of N.G.U. since there was little opportunity to study the antibody levels in patients with recently acquired infections. F. Hillman

667. Non-gonococcal Urethritis Contacts

J. A. BURGESS. *British Journal of Venereal Diseases* [Brit. J. vener. Dis.] 35, 24-26, March, 1959. 3 refs.

The author examined the female contacts of all new male patients attending three venereal disease clinics with non-gonococcal urethritis (N.G.U.), excluding those who developed N.G.U. while under surveillance for gonorrhoea. Of the 250 female contacts examined, 34% complained of vaginal discharge and 61% were symptom-free. More than 40% admitted to extra-marital intercourse during the preceding 3 months. In addition to clinical examination, smears and cultures were taken from the vagina, cervix, urethra, Skene's duct, and Bartholin's duct, and from the rectum where indicated. The presence of polymorphonuclear leucocytes in any of these sites was taken as evidence of an inflammatory process, and was found in 67% of cases. The underlying lesion was trichomoniasis in 34% and endocervicitis or cervical erosion, including a few cases of moniliasis, in 33%. No lesion was present in the remaining 33%.

On the strength of these findings it is suggested that cases of N.G.U. may be divided into three distinct groups, approximately equal in numbers: (1) those with venereally acquired trichomoniasis and moniliasis; (2) a second venereal group in which the female contact has endocervicitis or cervical erosion of a type distinct from the traumatic type found post partum and possibly due to a virus or virus-like organism; and (3) a non-venereal group including cases of N.G.U. associated with the ingestion of certain foods and drugs or due to chemical contraceptives or trauma to the urethral mucosa. The high proportion (33%) of healthy contacts found in this series supports the concept of a significant incidence of non-infective N.G.U. F. Hillman

Tropical Medicine

668. A Study of Pigmentation and Other Changes in the Liver in Malaria

T. SRICHAIKUL. *American Journal of Tropical Medicine and Hygiene* [Amer. J. trop. Med. Hyg.] 8, 110-118, March, 1959. 3 figs., 16 refs.

In the study here reported from Adulyadej Hospital, Bangkok, Thailand, the degree of hepatic involvement was judged by means of the thymol turbidity and iodine precipitation tests, using standard techniques, in 16 cases of malaria due to *Plasmodium falciparum* and 9 due to *P. vivax*. In addition liver biopsy was performed in 15 cases of the former group and in 8 of the latter, being repeated in 2 cases in each group 3 to 6 months after treatment.

Positive thymol turbidity reactions occurred in 15 of the falciparum cases and 8 of the vivax cases, while the iodine test results were positive in 7 of the former and in all the latter. On repetition of these tests in 2 cases of falciparum infection the thymol reaction became negative after 52 days in one patient but remained positive after 24 days in the other, who was jaundiced, while the result of the iodine test became negative in 9 and 24 days respectively. There was no relation between the degree of parasitaemia and the results of the hepatic function tests.

Liver biopsy was performed by the transthoracic approach in 14 of the falciparum cases, in 8 of the vivax cases and in 5 control subjects without malaria, specimens being taken from the patients between the 6th and 30th days from the first clinical attack, fixed in unbuffered formalin, and stained with haematoxylin and eosin. Malarial pigment was found in the Kupffer cells in 12 of the 14 falciparum cases (5 "long-standing" and one with jaundice) and in 7 of the vivax cases. It could be demonstrated as early as 6 days after the onset of a malarial attack and as long as 6 months after treatment, and was present in larger amounts in "chronic" cases. In 2 cases of falciparum and 2 of vivax malaria the amount of pigment present after 6 months was considerably less than at the original biopsy examination. No relation was apparent between the degree of parasitaemia, the amount of pigment, and the pathological changes observed.

B. G. Maegraith

669. Studies on Filariasis in Malaya: the Clinical Features of Filariasis Due to *Wuchereria malayi*

L. H. TURNER. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 53, 154-169, March, 1959. 1 fig., 44 refs.

Writing from the Institute for Medical Research, Federation of Malaya, the author reports that studies of filariasis due to *Wuchereria malayi* in endemic areas of Penang showed that the clinical features of "periodic" and "semi-periodic" forms of the disease were the same. Early stages were often symptomless, while enlargement of lymph nodes was not a consistent sign. Acute epi-

sodic adeno-lymphangitis was a common sign in later infections. Inflammation was often preceded by specially hard work or trauma, usually affected the leg, and never occurred at more than one site at a time. The fever lasted for 3 to 5 days and subsided rapidly, with much sweating. The distal part of the limb swelled on the 3rd day of the episode; swelling was progressively worse with each episode and eventually became permanent. Intervals between episodes were not regular; frequent attacks were commonly observed in patients with elephantiasis, but abscesses were uncommon. Elephantiasis usually occurred in the leg below the knee, was often bilateral, and sometimes developed insidiously in the absence of adeno-lymphangitis. Scrotal elephantiasis and hydroceles were rare.

The course of infection in Penang was irregular and unpredictable. Many carriers had no clinical signs of the disease, and microfilariae sometimes disappeared from the blood altogether. Repeated surveys of an untreated community showed little change in the microfilaria and elephantiasis rates from year to year. Most, if not all, of the people must have been infected at some time; the author suggests that elephantiasis may be caused by the development of allergy and by anatomical anomalies of the peripheral lymphatic system. In microfilaria surveys, in which 20 c.mm. of blood was withdrawn for examination, about 20% of infections were missed which were subsequently diagnosed by the febrile reaction which followed treatment with diethyl-carbamazine. No permanent sequelae occurred in patients who were treated in the early stages of the infection.

L. G. Goodwin

670. The Nodule in Onchocerciasis

M. S. ISRAEL. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [Trans. roy. Soc. trop. Med. Hyg.] 53, 142-147, March, 1959. 8 figs., 16 refs.

At the Department of Pathology, Royal College of Surgeons of England, London, 70 nodules removed from patients in Nigeria with onchocerciasis were examined histologically. Most of the adult worms in the nodules were disintegrating, while half of the nodules contained no living worms at all. Nodules from patients who had been treated with "antrypol" (suramin) 2 to 6 months previously contained the same proportion of dead worms as did nodules from untreated patients. The author considers that adult *Onchocerca* normally live freely in subcutaneous tissue. He supports the views of some earlier workers that nodules are formed in response to the release of substances (perhaps lipoids) from degenerating worms. The presence of well preserved portions of worm in some sections may, it is suggested, result from the trapping of healthy worms by the reaction caused by dying worms.

[The paper is illustrated by excellent photomicrographs.]

L. G. Goodwin

Allergy

671. Bronchial Asthma Due to Food Allergy Alone in Ninety-five Patients

A. H. ROWE, A. ROWE, and E. J. YOUNG. *Journal of the American Medical Association [J. Amer. med. Ass.]* 169, 1158-1162, March 14, 1959. 1 fig., 16 refs.

The authors believe that food allergy as a cause of asthma is overlooked because skin tests to foods are often negative and because the typical history is disregarded. They state that asthma which fluctuates in intensity, being severe for 2 to 3 days and then gradually subsiding over the next 5 days, with subsequent recurrence of the cycle, is characteristic, especially if it is worse in the winter and better or absent in the summer. Pyrexia up 104° F. (40° C.) is often present. Treatment with a diet free from all cereal grains, milk, eggs, chocolate, and fish is said to lead to improvement in many cases. Such improvement, however, may not begin for 3 or 4 weeks. Prolonged treatment, at least during the winter, is necessary for 1 to 4 years. Information relating to 50 children and 45 adults who are said to have responded to this form of treatment is given.

[The cases described have all the characteristics of infective allergy, and most physicians would consider infection to be the precipitating cause. The proof of food allergy rests on results of treatment alone and should be accepted with caution. No explanation is offered for the curious freedom from attacks in the summer months.]

R. S. Bruce Pearson

672. Bacterial Vaccines in the Treatment of Bronchial Asthma. [In English]

E. HELANDER. *Acta allergologica [Acta allerg. (Kbh.)]* 13, 47-66, 1959. 39 refs.

A number of workers have employed bacterial vaccines, particularly autogenous vaccines, for the treatment of patients in whom infection seems to play the predominating role in exacerbations of bronchial asthma. The average improvement rate in some 1,800 published cases was 71%, the figure for children being over 80%. A trial of bacterial vaccine in 308 cases of asthma provoked by respiratory-tract infection was carried out at Sahlgrenska Sjukhuset, Göteborg, Sweden, to find out (1) whether a stock or autogenous vaccine gave the better results; (2) the effect of age on results; (3) whether the effect differed with asthma of various degrees; (4) the effect of dose or duration of treatment; (5) whether local reactions altered the effect; and (6) the effect of placebo injections. It was found that somewhat better therapeutic effect was obtainable in the young than in the older asthmatic, but no other variable had any significant influence; particularly should it be noted that there was no difference between the results obtained with vaccine therapy and with injections of physiological saline.

The conclusions from these investigations are that the beneficial effects of treatment with bacterial vaccines in asthma provoked by infection are due to psychological

factors; and, as vaccines are not without some danger, they should be prescribed only in exceptional cases.

[This is an excellent paper and gives an answer to those who believe in the so-called specific effect of bacterial vaccines.]

A. W. Frankland

673. Respiratory Studies in Children. VI. Timed Vital Capacity in Healthy Children and in Symptom-free Asthmatic Children. [In English]

I. ENGSTRÖM, F. E. ESCARDÓ, P. KARLBERG, and S. KRAEPELIEN. *Acta paediatrica [Acta paediat. (Uppsala)]* 48, 114-120, March, 1959. 5 figs., 15 refs.

At the Paediatric Clinic of Karolinska Institutet, Stockholm, the ratio of the forced expiratory volume in one second (F.E.V._{1.0}) to the vital capacity (F.V.C.) was determined in 17 normal and 38 asthmatic children aged 6 to 14 years. The object of the trial was to discover whether, in the early stages of the disease, any bronchial obstruction persists in the period between attacks of asthma. The authors prefer to use the F.E.V._{1.0}:F.V.C. ratio as a measure of bronchial obstruction rather than either value individually because it is independent of body size.

Each child was tested at least 3 days after the last sign of asthma by means of an apparatus consisting essentially of a mouthpiece connected to a rigid airtight box of about 1,500 litres capacity, the pressure changes resulting from a maximum forced expiration into the box being measured by an electromanometer linked to a direct-writing recorder. The procedure was repeated 3 to 5 times at intervals of about one minute. The two records with the highest F.V.C. were then selected, the F.E.V._{1.0}:F.V.C. ratios calculated, and the mean taken.

The results for the asthmatic group were generally lower than those for the healthy group, the lowest values being found in the children having the most frequent attacks. The conclusion reached is that the signs of hyperinflation which are found between attacks of asthma in children are "at least partially dependent on a bronchial obstruction".

K. M. Hume

674. Triamcinolone in the Treatment of Allergic Conditions

L. H. CRIEP. *Journal of Allergy [J. Allergy]* 30, 50-60 Jan.-Feb., 1959. 6 figs., 29 refs.

The author reports, from the University of Pittsburgh, a trial of triamcinolone, a corticosteroid derived from prednisolone, in 250 patients suffering from various allergic disorders. The drug was given in an initial daily dose of 16 to 24 mg. which was progressively reduced to a maintenance dose of 2 to 12 mg. per day. With a daily maintenance dose of 10 mg. there was no sign of sodium retention, potassium depletion, or oedema. Other side-effects were about the same as with other corticosteroids. The potency of triamcinolone is approximately 1.5 times that of prednisone.

H. Herxheimer

Nutrition and Metabolism

675. Water and Electrolyte Exchanges of Obese Patients on a Reducing Regimen

R. PASSMORE, J. A. STRONG, and F. J. RITCHIE. *British Journal of Nutrition* [Brit. J. Nutr.] 13, 17-25, 1959. 1 fig., 4 refs.

The loss of weight of fat people on a reducing regimen is irregular. After a short period of rapid weight loss progress may slow down or come to a complete stop, even when the patient is cooperating fully. This is because the obese normally carry a moiety of body water which they lose early in the course of treatment by strict dieting (initial dehydration), but thereafter their relative body water content may increase (secondary water retention).

In this paper from the University of Edinburgh and the Western General Hospital the results are reported of water and electrolyte balance studies carried out on 5 obese patients during a strictly controlled reducing regimen lasting 6 weeks. Changes in the water intake appeared to be unrelated to the rate of loss of body water, and fluctuations in the urine output in most cases accounted only partially for variations in the total body water. Marked variations in evaporative water loss were noted, and in one patient they were more closely related to changes in the total body water than were changes in the urine output. It is suggested that the variable evaporative water loss might be associated with disturbances of temperature regulation. Studies of electrolyte exchange indicated that during the initial period of dehydration both intracellular and extracellular water was lost. Subsequent water retention was found to be associated with an increase in extracellular water, despite the probable continuing loss of intracellular water.

A. G. Mullins

676. The Effects of Exercise on Blood Cholesterol in Middle-aged Men

H. J. MONTROYE, W. D. VAN HUSS, W. D. BREWER, E. M. JONES, M. A. OHLSON, E. MAHONEY, and H. OLSON. *American Journal of Clinical Nutrition* [Amer. J. clin. Nutr.] 7, 139-145, March-April, 1959. 2 figs., 17 refs.

An investigation was carried out on 31 middle-aged male members of the faculty of Michigan State University, all sedentary workers, who were divided into a control group of 15 and an exercise group of 16. During the experimental period of 3 months the control subjects "followed their customary routine of activity", while the members of the exercise group were given supervised exercise. Three early-morning samples of blood were taken at weekly intervals from each subject at the beginning and end of the experiment for determination of the free and total cholesterol content.

In subjects whose serum cholesterol level was initially normal no change was observed after the period of

exercise, the mean initial and final levels showing no significant difference in either the "normal" exercise group (13 subjects) or the "normal" control group (13 subjects). In the 3 subjects with a high initial serum cholesterol level in the exercise group, however, an appreciable fall in the mean level was observed, which was greater than that in the 2 controls with a high initial level. But on further examination it was found that changes in the serum total cholesterol level in individual subjects were accompanied in all cases by changes in the body weight, regardless of whether the subject was in the exercise or in the control group. Thus while exercise was effective in reducing the serum total cholesterol level in some subjects, this effect appeared to be an indirect one connected with the reduction in weight.

[The diet was neither controlled nor accurately recorded in these investigations.] Z. A. Leitner

METABOLIC DISORDERS

677. Studies of the Intestinal Flora in Sprue: the Effects on the Syndrome of Its Modification with Various Diets and with Lactose. (Estudios sobre la flora intestinal en el esprue: sus modificaciones y efectos sobre el síndrome con dietas diversas y con lactosa)

C. JIMÉNEZ DÍAZ, C. MARINA, J. M. ROMEO, E. ORTIZ MASLLORENS, J. M. ALÉS, and M. AGUIRRE. *Revista clínica española* [Rev. clín. esp.] 72, 303-308, March 15, 1959. 5 figs., 7 refs.

The effect of various diets on 4 patients with sprue was studied at the Institute of Clinical and Medical Investigation, Madrid. It was confirmed that there is a reduction in the amount of faecal fat when a gluten-free diet is given instead of a normal basal diet, and it was shown that the oral administration of lactose in doses of 10 to 30 g. daily leads to a further reduction in faecal fat content, the faecal lactobacillus count increasing in 3 of the 4 patients at the same time. It is considered that lactose acts primarily on the intestinal flora, increasing the number of lactobacilli present, and that the reduction in faecal fat content follows this change.

Kenneth Gurling

678. Some Observations on the Malabsorption Syndrome, Based on the Use of Absorption Tests and Biopsy of the Small Intestine

P. J. CULVER, J. A. BENSON, E. STRAUSS, and C. M. JONES. *Gastroenterology* [Gastroenterology] 36, 459-466, April, 1959. 6 figs., 13 refs.

In 7 cases of the malabsorption syndrome the histological appearance of surgical biopsy specimens of the jejunum were compared with those of jejunal biopsy specimens obtained with the peroral tube described by Shiner (*Lancet*, 1956, 1, 85). The material was obtained

at the Massachusetts General Hospital, Boston, from 7 patients showing malabsorption on whom laparotomy was performed, surgical biopsy specimens of a segment of the upper jejunum being taken. In 3 of these cases the Shiner tube was passed before the surgical biopsy and a specimen was taken from the same area of the jejunum. The specimens were immediately fixed in the operating room in 10% formalin.

The histological appearances of the jejunal mucosa were abnormal in all the specimens. There was similarity between the histology of the surgical biopsies and that of the Shiner-tube biopsies. The final diagnoses were: Whipple's disease (2 cases), reticulum-cell sarcoma (1 case), islet-cell carcinoma of the pancreas (1 case), and sprue (3 cases). The diagnoses in the cases from which both types of biopsy specimen were taken were: Whipple's disease (1 case) and sprue (2 cases). In the patients with sprue atrophic villi and disorderly columnar epithelium with cuboidal epithelial cells and round or pyknotic nuclei were prominent features, but it is not yet known whether these abnormalities are specific for sprue. There was no consistent relationship between the severity of histological abnormalities and the severity of malabsorption as determined by biochemical tests.

Joseph Parness

679. **Acute Intermittent Porphyrism: a Study of 50 Cases**
A. GOLDBERG. *Quarterly Journal of Medicine* [Quart. J. Med.] 28, 183-209, April, 1959. 7 figs., bibliography.

The author has made a study of the clinical features of 50 cases of acute intermittent porphyria in which he has attempted to assess aetiological factors, including the genetic factor, and the mechanism involved in the production of symptoms and signs. Of the 50 patients (31 females and 19 males), 19 had one or more relatives with the same disease in an active or a latent form, the latent cases being discovered by the demonstration of porphobilinogen in the urine by a chromatographic method. It was noted that even in the established cases the excretion of porphobilinogen was not constant, so that its absence was not considered to exclude the latent stage in relatives. A study of the families of 11 patients gave results consistent with the hypothesis that the trait is inherited as an irregular Mendelian dominant character.

In 3 cases prolonged administration of barbiturates apparently precipitated attacks. Of 31 cases with paralysis, 24 (77%) had been given barbiturates, whereas of 17 patients without paralysis, 6 (35%) had taken barbiturates. In all 4 cases treated with quinalbarbitone quadriplegia ensued. In several cases infections preceded attacks, and in some others pregnancy was a precipitating factor.

Abdominal pain, either alone or associated with vomiting, constipation, or more rarely diarrhoea, was the commonest presenting symptom. In 11 cases (22%) neurological or psychological symptoms were predominant, and 3 patients (6%) presented with epileptic fits. During the attacks severe abdominal pain, vomiting, diarrhoea, and loss of weight were prominent features. In 34 cases there was paralysis of limb muscles,

and 28 had quadriplegia. The paralysis was mostly of the lower motor neurone variety, but 5 patients had extensor plantar responses. Cranial nerve lesions were present in 14 cases, epileptic fits in 8, pain in the limbs in 26, and impaired sensation in 19. Six cases had incontinence of urine and 5 respiratory paralysis. Tachycardia was noted in 32 cases and transient hypertension in 27, with a return to normal when improvement took place. Mental symptoms such as depression and confusion occurred in 29 cases, and 6 patients were certified insane.

There were 12 fatal cases, the cause of death being paralysis, in most cases with terminal respiratory infection. In 6 cases in which post-mortem examination was performed the findings were non-specific with the exception of foci of demyelination in peripheral nerves and the brain and the demonstration of porphobilinogen in the liver and kidneys.

Corticotrophin was given to 5 patients, with some improvement in only 2. Improvement was also noted in 2 of 4 patients treated with cortisone. Neostigmine, which was given to 5 patients, had no effect on either paralysis or pain. Treatment was otherwise symptomatic, with particular attention to respiratory paralysis and electrolyte disturbances. It is recommended that barbiturates should be withheld in all established cases, and from the patients' relatives.

The author suggests that the basic abnormality in acute porphyria is a disturbance of pyrrole pigment metabolism in the liver and nervous system.

Charles Rolland

680. **Overweight in the Aged**

G. HOLLIFIELD and W. PARSON. *American Journal of Clinical Nutrition* [Amer. J. clin. Nutr.] 7, 127-131, March-April, 1959. 1 fig., 5 refs.

From the University of Virginia School of Medicine, Charlottesville, an analysis is reported of the body weight of 681 subjects (474 male and 207 female) over the age of 65 years who were either attending an out-patient clinic or resident in homes for the aged in Virginia. Less than 10% were negroes, and all were ambulatory and free from debilitating disease.

It was found that 11% of the males and 15.9% of the females were 20% or more above the average weight for height and age. Further, 10.9% of the males and 8.2% of the females were 20% or more above the average weight of subjects in the age group 55 to 59 years as presented in the average weight tables used by insurance companies. The proportion of subjects over 65 years who were 20% or more overweight was at least equal to that in the general population. Average weight tended to fall after the age of 75. A study of the history of the patients over 65 indicated that for those within 20% of average weight at the time of investigation, 30.9% of the females and 25.5% of the males had at some previous time exceeded the average weight by 20% or more.

It is concluded that the incidence of obesity in this age group is as great as or greater than that in young adults.

A. G. Mullins

Gastroenterology

681. Fever of Obscure Origin—the Value of Abdominal Exploration in Diagnosis. Report of Seventy Cases

J. E. GERACI, L. A. WEED, and D. R. NICHOLS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 169, 1306–1315, March 21, 1959. 18 refs.

The diagnostic value of laparotomy in patients with fever of obscure origin was studied at the Mayo Clinic, the subjects being 41 males and 29 females, aged 1 to 71 years (average 48 years), with fever of more than 3 weeks' duration. No cause for the febrile state could be found on repeated clinical examination or in the results of laboratory investigations, but organic disease was suspected. At operation malignant disease was diagnosed in 21 cases, including lymphoid tumour in 10. Specific infections, including tuberculosis in 5, histoplasmosis in 2, and brucellosis in 2, were diagnosed in 15 cases. Miscellaneous conditions were found in 6 cases, periarteritis nodosa being present in one of these and cholelithiasis in 2. In another group of 14 cases inflammatory lesions of uncertain aetiology, but mostly granulomatous in character, were discovered. In the remaining 14 patients in the series the findings were entirely negative.

[The diagnostic value of laparotomy in this series is impressive, but it should be noted that in no fewer than 40 cases there were subjective or objective features referable to the abdomen.]

A. Wynn Williams

682. Lesions of the Small Intestine and Ulcerative Rectocolitis. (Lésions de l'intestin grêle et rectocolite ulcéro-hémorragique)

J. LOYGUE, R. FLORENT, and R. GOT. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] 48, 308–322, April, 1959. 6 figs., 10 refs.

It was formerly believed that the lesions of ulcerative colitis were strictly confined to the colon and rectum and that the ileo-caecal valve was the absolute limit in topography. The present authors agree with others that this dictum can no longer be regarded as true and that the same pathological condition may extend into the ileum. Among 34 cases of ulcerative colitis treated surgically they have found involvement of the terminal ileum at operation or at necropsy in at least 8.

The lesions of the small intestine which may be observed in cases of ulcerative colitis are of three types. (1) Ileitis, either retrograde or due to regurgitation. This rarely extends more than 10 to 15 cm. above the valve and its presence may be detected only by radiology. The prognosis is not bad and excision of the affected segment is not called for. (2) Crohn's disease—follicular and segmentary enteritis—which may precede, follow, or co-exist with ulcerative colitis. The exact relationship between the two diseases remains so far undetermined. (3) Postoperative ileitis, caused by obstruction. This is

simply a surgical complication due to the shortening effected by ileostomy or ileo-rectal anastomosis.

[A very interesting and full report of the discussion which followed this communication to the Société Nationale Française de Gastro-Entérologie, especially in relation to the association between ulcerative colitis and Crohn's disease, is published in the same issue (pp. 331–333) and should be read in association with it.]

J. W. McNee

683. Ulcerative Colitis. Treatment and Prognosis Studied on the Basis of 161 Cases. [Monograph, in English]

J. LINDENBERG. *Acta chirurgica Scandinavica* [*Acta chir. scand.*] Suppl. 236, 1–118, 1958. 14 figs., bibliography.

STOMACH AND DUODENUM

684. Pyloric Stenosis

J. A. BALINT and M. P. SPENCE. *British Medical Journal* [*Brit. med. J.*] 1, 890–894, April 4, 1959. 2 figs., 15 refs.

The authors have made a study of pyloric stenosis based on the records of 118 patients (86 men and 32 women) discharged from the Central Middlesex Hospital, London, with that diagnosis. Major and minor diagnostic criteria for inclusion in the study are described.

Benign prepyloric and pyloric ulcers were classified as duodenal because distinction was impossible, and on this basis duodenal ulceration was the cause of stenosis in 95 cases. A gastric ulcer remote from the pylorus caused the obstruction in 7 cases, a mass of fibrous tissue extending along the lesser curvature and enveloping the pylorus. Carcinoma of the pyloric antrum was responsible in 13 cases, kinking of the duodenum with adherence to a chronically inflamed gall-bladder in 2, and a congenital diaphragmatic constriction at the pylorus in the remaining case. The age and sex distribution of the various diagnostic groups is given.

Vomiting due to the stenosis occurred in 115 cases, and 105 patients complained of pain. Anorexia was present in 73 cases. A weight loss of 5 lb. (2.26 kg.) or more was reported in 77 cases, including 18 with a weight loss greater than 27 lb. (12.24 kg.) and 23 greater than 13 lb. (5.89 kg.). Diarrhoea with offensive eructations occurred in 23 cases, excluding those with an obvious cause such as idiopathic steatorrhoea or sensitivity to antacids, and was the presenting feature in 6 cases. The first symptoms (usually pain, sometimes perforation or haemorrhage) attributable to duodenal ulceration preceded admission for pyloric stenosis by 10 or more years in 53 cases and by less than 5 years in only 18. If the first symptom of gastro-duodenal disease occurred less than a year before admission for pyloric stenosis there

was an almost even chance of malignancy. The three signs mainly associated with pyloric stenosis were succussion splash (66 cases), visible gastric peristalsis (33), and dehydration (29). Barium-meal examination, carried out on 93 patients, showed evidence of delayed emptying in 79. Anaemia was common and a raised haemoglobin level rare.

Difficulties in immediate diagnosis were encountered in one-third of the cases admitted as emergencies owing to the prominence of symptoms such as excessive pain and haematemesis. Of the 95 patients with pyloric stenosis due to duodenal ulcer, 68 were treated by partial gastrectomy and 20 elderly patients by gastro-enterostomy. Four were treated medically, but 3 of these required surgery within 9 months. The remaining 3 died before surgery was possible. Of the 7 patients with gastric ulceration, 4 were treated surgically and one died before operation was possible. The 2 remaining patients were treated medically, but one required surgery after 3 years and the other died from emphysema 2 years later. Of the 13 patients with carcinoma, 11 were treated by surgery and one died before operation was possible. The remaining patient, thought to have a duodenal ulcer, was unexpectedly found to have a carcinoma during surgical treatment. Both the patients with adhesions had the duodenum freed from the chronically inflamed gall-bladder, but one subsequently died from cerebral thrombosis. In the case of congenital diaphragmatic constriction this was only found at necropsy following a fatal pulmonary embolism.

The authors compare their findings with other published reports. It would seem that about 2% of patients with a benign peptic ulcer ultimately develop pyloric stenosis severe enough to satisfy the authors' stringent criteria. This figure would be higher if cases of peptic ulcer in which a medical regimen has failed were not treated surgically before the onset of obstructive symptoms.

In brief the authors state that their study of pyloric stenosis has confirmed previous descriptions of the disease apart from the 20% incidence of diarrhoea in their cases. Surgical therapy is unequivocally indicated.

J. Warwick Buckler

685. Effect of Smoking on Gastric Secretion

D. W. PIPER and J. M. RAINE. *Lancet* [Lancet] 1, 696-698, April 4, 1959. 3 figs., 15 refs.

In view of the demonstration by Doll *et al.* (*Lancet*, 1958, 1, 657; *Abstr. Wld Med.*, 1958, 24, 184) that smoking may be a factor in the production and maintenance of peptic ulcer, the present authors have investigated, at the University of Sydney, Australia, the effect of smoking on gastric secretion in 12 subjects, all smokers, of whom 3 had peptic ulcer, 3 were healthy students, and 6 had diseases unrelated to gastric function. The investigation involved two separate experiments: (1) a smoking experiment, in which the basal gastric secretion was studied in the first hour, the secretion in response to 4 to 6 cigarettes was studied in the second hour, and the maximum secretory response to histamine was estimated during the third hour; and (2) a control experiment, in which the basal fasting

secretion in the same subjects was studied for 2 hours, none having smoked in the 10 hours preceding the tests.

In the first experiment the smoking of 4 to 6 cigarettes was accompanied by a significant increase in the volume, free acid, total acid, and chloride content of the gastric secretion. In the control experiment, however, there was a significant decrease in all of these values for the gastric secretion during the second hour of the test. When the results of the smoking experiment were recalculated in relation to the downward trend of the basal secretion during the second hour of the control test the extent of the stimulation produced by smoking was still more manifest: thus the free and total acid secretion were shown to be increased by over 100%. Further analysis of the results showed that both the parietal and non-parietal cell components of the gastric secretion were stimulated. The results of similar previously recorded studies are discussed and reasons suggested why some earlier investigators have supported the above conclusions but others have not. In view of the variable reactions to smoking of different patients the present authors attach importance to the use of each subject as his own control.

Joseph Parness

LIVER AND GALL-BLADDER

686. Serum Glutamic Oxalacetic Transaminase and Iron in the Differential Diagnosis of Jaundice

F. GOLDSTEIN, D. SELIGSON, and H. L. BOCKUS. *Gastroenterology* [Gastroenterology] 36, 487-500, April, 1959. 4 figs., 32 refs.

The diagnostic value of the serum iron and the serum glutamic oxalacetic transaminase (S.G.O.T.) levels in jaundice was studied at the Graduate Hospital of the University of Pennsylvania, Philadelphia, in 100 jaundiced patients (46 male and 54 female), including 21 negroes. In all cases a full clinical examination and a battery of liver function tests were carried out, and in all except 3 a firm clinical diagnosis was made.

The patients with jaundice due to viral hepatitis were divided into two groups: (1) those with the "orthodox" type, in which the reaction to the serum flocculation test was markedly positive and the serum alkaline-phosphatase level was normal or only moderately raised; and (2) those with the "cholestatic" type, in which the reaction to the flocculation test was negative or "barely positive" and the alkaline-phosphatase level was markedly raised.

In cases of orthodox hepatitis there was a good correlation between the rate of fall of the serum bilirubin level and the return to normal of the serum iron and S.G.O.T. values. Almost the same correlation was observed in cases of cholestatic hepatitis, but in 3 patients the serum iron level returned to normal more slowly. In patients with jaundice due to a block in the extra-hepatic biliary system there was no correlation between the serum bilirubin and the serum iron or S.G.O.T. levels, and although the results of liver function tests did not help in differentiating between extrahepatic biliary obstruction and cholestatic hepatitis the S.G.O.T.

and serum iron levels were consistently valuable in the differential diagnosis of these two conditions. Both the S.G.O.T. and the serum iron values were increased in cholestatic hepatitis and normal or slightly elevated in extrahepatic biliary obstruction.

In general, S.G.O.T. activity was higher in hepatitis with cholestasis than in extrahepatic biliary obstruction, and the highest values were obtained in the orthodox type of hepatitis. There was little difference between the serum iron level in patients with orthodox hepatitis and that in patients with cholestatic hepatitis, but there was a clearer differentiation between either type of hepatitis and extrahepatic biliary obstruction. The S.G.O.T. value was very high in 2 patients with hepatic cirrhosis complicated by jaundice, in both of whom massive necrosis of liver cells was found at necropsy.

Discussing these findings the authors suggest that a rise in the serum iron level may be due to hepatic necrosis and occasionally to other factors such as the presence of a haemolytic component. S.G.O.T. activity also depends on several variables, and the mechanism by which it is increased in liver disease is discussed, the conclusion being that it is related to the amount of liver cell necrosis. Although the serum iron and S.G.O.T. levels may be raised in hepatitis, they occasionally rapidly return to normal while the patient is still icteric; this must be borne in mind when there appears to be a dissociation between jaundice and normal values for S.G.O.T. and serum iron.

It is considered that estimation of both the serum iron and the S.G.O.T. levels in patients with jaundice helps to eliminate difficulties due to an abnormal value for either alone from other causes. High values for both are diagnostic of liver cell damage and a combined value for S.G.O.T., expressed in units per ml., and of serum iron, expressed in $\mu\text{g. per } 100 \text{ ml.}$, of over 400 probably indicates acute hepatitis, either orthodox or cholestatic. Determination of these levels is of greatest value in the detection of cholestatic hepatitis when the results of other liver function tests are not helpful.

A. E. Read

687. Serum Transaminases in Hepato-biliary Disease. (Les transaminases du sérum en pathologie hépatobiliaire)

P. BOIVIN, R. BESSON, L. HARTMANN, and R. FAUVERT. *Revue française d'études cliniques et biologiques* [Rev. franç. Ét. clin. biol.] 4, 349-362, April, 1959. 11 figs., bibliography.

From the Hôpital Beaujon and the Institut National d'Hygiène, Paris, the authors report the results of more than 500 determinations of serum glutamic oxalacetic transaminase (S.G.O.T.) and serum glutamic pyruvic transaminase (S.G.P.T.) activity in patients with hepatobiliary diseases and in normal controls. Their findings correspond in general to those of other workers. There was an enormous increase in the serum content of both enzymes during the first 10 days of viral hepatitis with a progressive fall thereafter, a secondary rise or a failure to fall suggesting persisting activity. High values were found more constantly in post-hepatitic cirrhosis than in alcoholic cirrhosis or haemochromatosis

(in which the S.G.P.T. content was often normal). Moderate elevations in the level of both enzymes were found in primary and secondary carcinoma of the liver, in obstructive jaundice due to cancer, and in cholelithiasis during exacerbations of the cholangitis. There was little correlation between the serum enzyme values and the results of other biochemical tests of liver function. It is concluded that for the study of hepatobiliary disease the determination of S.G.O.T. activity is the more sensitive test, but that of S.G.P.T. activity is more specific.

P. C. Reynell

688. Cirrhosis in Women: a Clinicopathologic Study

L. G. STUHLER, A. H. BAGGENSTOSS, and H. R. BUTT. *Gastroenterology* [Gastroenterology] 36, 467-479, April, 1959. 5 figs., 43 refs.

To determine whether the natural history of cirrhosis of the liver in females is significantly different from that in males the authors studied the aetiological, pathological, and clinical features of portal cirrhosis in 86 white female patients seen at the Mayo Clinic between 1924 and 1954. Necropsy was performed in all cases, constituting 1.6% of all necropsies on female patients during this period. Patients with cirrhosis associated with biliary obstruction, haemochromatosis, or heart failure were excluded.

Pathologically, the lesions were of the post-necrotic type in 73 cases and the Laënnec type in 13. The patients with post-necrotic cirrhosis were, on the average, 10 years younger than those with the Laënnec type, and in 37 of them the cirrhosis was thought to be due to a previous attack of viral hepatitis. The cause of the cirrhosis in 22 of the post-necrotic group could not be ascertained. About one-quarter of those developing cirrhosis after an attack of hepatitis did so within 3 years. The second commonest cause of the post-necrotic lesion was exposure to chemical agents, such as arsenic or cinchophen. The commonest cause of the Laënnec type of cirrhosis was a heavy intake of alcohol.

The symptomatology in both types of cirrhosis was similar, and included disturbances of menstrual function and arthralgia. In view of the known association between arthralgia and cirrhosis in young women, it was of interest that only 3 of the 11 patients suffering from joint symptoms were under 40 years of age. On physical examination the liver was palpable more often in patients with cirrhosis of the Laënnec type than in the group with post-necrotic cirrhosis, but there was no significant difference between the two groups in the results of liver function tests or the cause of death, which was usually intercurrent infection, hepatic coma, or gastrointestinal haemorrhage. Primary carcinoma of the liver developed in only one patient in the series.

Macroscopically, the liver in the post-necrotic group appeared as a small, reddish-brown organ with a coarse cirrhosis and large regeneration nodules. Atrophy of a lobe or portion of a lobe was common in this group, and in most cases the weight of the liver was 60% or less of the weight of the normal liver. Microscopically, there were broad bands of connective tissue separating irregular nodules. Fatty change in the liver cells was slight and bile-duct proliferation marked. A subgroup of

the post-necrotic series had a granular liver with a fine cirrhosis. This lesion was commonest in those cases in which hepatotoxic drugs seemed to have been responsible for the cirrhosis, but it was also seen in 9 patients with a history of previous viral hepatitis. The authors consider that, microscopically, this type of cirrhosis could be differentiated from the Laënnec type, which it resembled macroscopically, by the varying size of the regeneration nodules and the fact that nodules were often confluent, presenting a "garland-like" appearance.

In the patients with Laënnec cirrhosis the liver was yellow and fatty, was heavier than the normal liver, and had a fine granular appearance. Microscopically, the nodules were small, with thin surrounding bands of fibrous tissue, and there were marked fatty changes in the liver cells.

From these observations the authors conclude that: (1) cirrhosis in young women is frequently of the post-necrotic type, in marked contrast to cirrhosis in older females and in males, which is commonly of the Laënnec (alcoholic) type; (2) viral hepatitis is the most important causative factor in post-necrotic cirrhosis; and (3) viral hepatitis and chemical agents may cause a fine granular type of cirrhosis which can be distinguished microscopically from the alcoholic type. *A. E. Read*

689. The Use of Radioactive (I^{131} -labeled) Rose Bengal in the Study of Human Liver Disease: Its Correlation with Liver Function Tests

C. H. LUM, W. J. MARSHALL, D. D. KOZOLL, and K. A. MEYER. *Annals of Surgery [Ann. Surg.]* 149, 353-367, March, 1959. 13 figs., 10 refs.

The authors have evaluated the use of rose bengal labelled with radioactive iodine (I^{131}) in testing liver function. Tests were performed on 231 patients at the Cook County Hospital, Chicago; 183 of these were suffering from cirrhosis, infective hepatitis, calculous obstruction, or carcinoma obstructing the extrahepatic ducts, and the remaining 48, with no liver disease, served as controls. The diagnosis was either confirmed histologically or was considered certain because of unequivocal clinical findings with biochemical confirmation. The tests were carried out as follows. After intravenous injection of 5 μ c. of I^{131} -labelled rose bengal solution (containing 5 mg. of the dye) radioactivity over the liver was measured by a shielded scintillation counter until a peak counting rate was reached (between 30 and 90 minutes after injection), and at this time a blood sample was also taken and its radioactivity measured. At 6 and 24 hours after injection the radioactivity over the liver and in the plasma were again measured. Detailed analyses of these measurements are presented, with statistical analysis of the correlation of the results both with the clinical diagnosis and with the results of biochemical tests of liver function. On this basis the authors suggest that the combination of liver and blood radioactivity measurements immediately after injection and 24 hours later is of considerable diagnostic value. It is also suggested that the test may be adapted to assist measurement of liver cell mass and liver blood volume.

K. E. Halnan

PANCREAS

690. Simplified Screening Test for Cystic Fibrosis of the Pancreas

E. M. KNIGHTS, J. S. BRUSH, and J. SCHROEDER. *Journal of the American Medical Association [J. Amer. med. Ass.]* 169, 1279-1280, March 21, 1959. 1 fig., 3 refs.

In children an increase in the chloride concentration in sweat, accompanied by relevant clinical findings, is usually considered strongly suggestive of cystic fibrosis of the pancreas. In this paper from Hurley Hospital, Flint, Michigan, a rapid screening method for the diagnosis of this disease is described. Hand test papers were made with filter paper impregnated with silver chromate, white silver chloride being precipitated upon contact with sodium chloride solution. The method was tried on 91 healthy subjects and 9 patients with cystic disease of the pancreas; a 3+ reaction was obtained in all the patients with pancreatic disease. Relatively strong reactions were also given by the parents of some diseased children. In some emotional and febrile children false positive reactions occurred.

The authors state that the test papers are easy to prepare and to store and after use can be kept as permanent records.

A. Wynn Williams

691. Urine Diastase in the Evaluation of Pancreatic Disease

J. J. BUDD, K. E. WALTER, M. L. HARRIS, and W. A. KNIGHT. *Gastroenterology [Gastroenterology]* 36, 333-353, March, 1959. 25 figs., 43 refs.

The authors, in an investigation at the St. Louis (Missouri) School of Medicine, have re-evaluated the significance of urinary diastase determination in the diagnosis of pancreatic disease. Both serum and urinary diastase values were determined by the iodometric method of Somogyi. Normal serum diastase levels had previously been established by the authors in healthy medical students, and these figures, together with the results of 107 urinary diastase estimations performed on 26 medical students and 27 control patients without pancreatic disease, are compared with the findings in 25 patients suffering from disease of the pancreas, 10 of whom had acute pancreatitis. The results of serial estimations and the clinical findings are given in detail for each patient.

In acute pancreatitis the serum diastase level followed the expected pattern, being initially raised and falling rapidly to normal, while the urinary diastase value remained persistently high for longer periods, and it is suggested that this may facilitate diagnosis in patients first seen several days after the onset of the condition. Variable results were obtained in chronic pancreatitis and after surgical procedures on organs in the pancreatic area. Again the urinary diastase level was more consistently elevated than the serum level. Six cases of carcinoma of the head of the pancreas were investigated, in one of which serum and urinary diastase values were high after partial pancreatectomy; in the other 5 cases both serum and urinary levels were low.

T. D. Kellock

Cardiovascular System

692. Blood Pressure and Obesity

H. M. WHYTE. *Circulation* [Circulation] 19, 511-516, April, 1959. 2 figs., 11 refs.

At Sydney Hospital, Australia, the relationship between blood pressure and obesity was studied in 100 healthy males aged 30 to 40 years. Blood pressure, which was recorded when the subjects attended the hospital for blood donation, was not necessarily basal. A brace-and-clip sphygmomanometer cuff of standard width (13 cm.) was preferred to the sleeve pattern. Age, height, weight, circumference of the arm, and the serum cholesterol concentration were recorded, and obesity was estimated from the aggregate skin-fold thickness at three sites (para-umbilical, over the triceps, and over the inferior angle of the scapula).

Both systolic and diastolic pressures were found on correlation analysis to be positively associated with body weight, obesity, and arm circumference, but since the last three values were themselves inter-correlated, partial correlation and regression methods were used to determine their relative importance. When other factors were held constant only the influence of weight remained significant, an increment of 28 lb. (12.7 kg.) corresponding to an average rise of 10 mm. Hg in systolic pressure and 7 mm. Hg in diastolic pressure. The serum cholesterol level increased significantly with age, but neither of these factors appeared to be related to blood pressure. Height had a slight negative effect with constant weight, suggesting that bulk was more important than absolute weight.

It is concluded that alterations in body bulk influence blood pressure, regardless of whether fat or muscle is the tissue chiefly concerned. Obesity has only an indirect effect, through its contribution to total weight. Arm circumference, as measured in this group of subjects, is unrelated to blood pressure, though this discrepancy with previous findings may be connected with the type of cuff employed.

S. G. Owen

693. Polythelia in Cardio-arterial Disease

W. EVANS. *British Heart Journal* [Brit. Heart J.] 21, 130-136, Jan., 1959. 4 figs., 12 refs.

Polythelia, or the presence of accessory nipples, was sought in 2,000 consecutive patients attending [the London Hospital] for examination of the heart. Some form of cardioarterial disorder was discovered in 941 of them, while the remaining 1,059 cases showed neither disease of the heart nor of any other system. The incidence of polythelia among the healthy group proved to be 5%.

Among those with cardioarterial disease, polythelia was common in three clinical states. Thus, it was present in 35% of patients with systemic hypertension showing contracted arteries, left ventricular enlargement, and left ventricular preponderance in the electro-

cardiogram, but in only 5% of subjects with systemic hypertonia, where the blood pressure was raised to impressive levels but where cardioarterial derangement, including left ventricular preponderance in the electrocardiogram, was absent.

Next, the incidence of polythelia was 44% in congenital cardiac shunts, mitral stenosis, or emphysema, when pulmonary hypertension was present, producing right ventricular hypertrophy and right ventricular preponderance in the electrocardiogram. In these same clinical states when the pulmonary arterial pressure might be raised, but where no right ventricular preponderance appeared in the electrocardiogram, representing a state of pulmonary hypertonia, the incidence of polythelia was only 7%.

Polythelia was also a common finding (44%) among patients with cardiomyopathy arising from a myocardial affection other than coronary arterial disease, and assuming the form of either myocarditis or a tardy fibrosis.

Since polythelia is a manifestation of atavism, its association with any particular disease suggests for it a genetic or congenital basis. Its high incidence in systemic hypertension, pulmonary hypertension and cardiomyopathy suggests for these three clinical states a congenital predisposition.—[Author's summary.]

694. The Effect of Lipemia upon Coronary and Peripheral Arterial Circulation in Patients with Essential Hyperlipemia

P. T. KUO, A. F. WHEREAT, and O. HORWITZ. *American Journal of Medicine* [Amer. J. Med.] 26, 68-75, Jan., 1959. 3 figs., 27 refs.

Rapid changes in the blood lipid levels were induced by manipulation of the dietary fat intake in 6 patients with essential hyperlipemia and clinical atherosclerosis. Studies were then made to correlate the changing blood lipid values with subjective and objective findings of cardiac and peripheral ischemia in each of these patients. The patients' symptoms and signs of arterial ischemia showed prompt improvement with clearing of the lipemia. Reinstitution of high fat feeding for 7 to 21 days returned all the patients to the state of hyperlipemia and to the same clinical status of their control or full diet period. It was found that in a given patient, manifestations of arterial insufficiency could be correlated, although roughly, with the rise and fall of the serum triglyceride level. Evidence was found to indicate that hyperlipemia may, in certain patients, affect the oxygenation of arterial blood. It is suggested that this effect of lipemia in the coronary and peripheral arteries might interfere with the diffusion of an adequate amount of oxygen from the blood to meet the requirement of the tissues that are supplied by a diseased vessel. The data reported in this present investigation add confirmative evidence to earlier

observations that lipemia may be one of the factors that aggravates or precipitates acute arterial insufficiency in arteriosclerotic subjects. Satisfactory control of lipemia is therefore indicated in patients with severe coronary and peripheral vascular diseases.—[Authors' summary.]

695. **A Study of Early Venous Return in Obliterating Arteritis of the Lower Limbs.** (Étude du retour veineux précoce dans l'artérite oblitérante des membres inférieurs) R. LEGRAND, J. VANDECASTEELE, J. DESRUELLES, P. FOSSATI, A. GERARD, and R. GOURDIN. *Presse médicale* [Presse méd.] 67, 598-599, March 25, 1959. 3 figs., 2 refs.

During the arteriographic study of 81 cases of obliterating arteritis at the Medical Clinic of the Lille Faculty of Medicine unusually early venous return of the medium was noted on 19 occasions. This rapid transfer of blood to the veins may result from the opening of arteriovenous communications and may thus form part of the circulatory disturbance diverting blood from the distal parts of the limb. In 10 of the 19 cases the deep muscle temperature in the affected part of the limb near the main occlusion was measured, and was found in 7 to be abnormally high (37° C.), suggesting the rapid passage of arterial blood.

J. McMichael

CONGENITAL HEART DISEASE

696. **Atrial Septal Defect: Factors Affecting the Surgical Mortality Rate**

D. C. MCGOON, H. J. C. SWAN, R. O. BRANDENBURG, D. C. CONNOLLY, and J. W. KIRKLIN. *Circulation* [Circulation] 19, 195-200, Feb., 1959. 7 refs.

The authors have studied 119 adults operated on at the Mayo Clinic before January, 1958, for repair of atrial septal defects, patients with ostium primum defects and associated cardiac abnormalities (other than partial anomalous venous drainage of the right lung) having been excluded. Of the 119 patients, 108 were operated on by the "atrial well" technique, 7 by open cardiectomy with extracorporeal circulation, and 4 by the Bailey technique. There were 14 operative deaths (12%), in only 2 of which were there obvious contributory technical factors. Age *per se* had no influence on operative mortality. Factors which significantly increased the mortality rate were: (1) a clinical history of congestive heart failure; (2) a markedly raised right atrial pressure; (3) a large right-to-left shunt; (4) marked elevation of the pulmonary arterial pressure; and (5) markedly increased pulmonary vascular resistance. In 80 cases presenting none of these features the operative mortality was 1.3%; in 9 cases where 2 factors were present it was 56%; and in 2 cases with all 5 factors there was 100% mortality.

Because of the low operative risk established in the large group of patients (108) operated upon by the atrial well technique the authors feel justified in advising that an atrial septal defect of significant size be repaired by this method even in patients with no or only minimal symptoms.

F. J. Sambrook Gowar

697. **Cardiac Surgery in the Newborn. Experience with 120 Patients under One Year of Age**

H. A. COLLINS, F. J. HARBERG, L. R. SOLTERO, D. G. McNAMARA, and D. A. COOLEY. *Surgery* [Surgery] 45, 506-519, March, 1959. 1 fig., 31 refs.

The authors report in detail a series of 120 infants under the age of one year who were operated on for congenital malformations of the heart or great vessels at the Children's Hospital, Houston, Texas, during the last 4 years; 13 of these patients were aged under one month. In 38 cases a heart-lung machine was used, and all the operations were performed as an emergency or semi-emergency because of impending heart failure.

Among 29 cases of ventricular septal defect (in all of which the heart-lung machine was used) there were 12 deaths, a mortality of 41%; among 28 cases of the tetralogy of Fallot (Blalock's operation being performed in 14 and Pott's operation in 14) there were 22 survivors, with improvement in 19; of 17 cases of transposition of the great vessels, an atrial septal defect was created in 13, with improvement in 9. There were 14 cases of coarctation of the aorta; the 4 patients with preductal coarctation all died, but all 10 cases of postductal coarctation were operated on with good result. Tricuspid valvular atresia occurred in 10 cases and was treated by Blalock's operation in 5 and by Potts's operation in the other 5, with a satisfactory result in 7 cases. The other conditions included patent ductus arteriosus (9 cases with 3 deaths), congenital aortic stenosis (4 cases, no deaths), congenital pulmonary stenosis (also 4 cases and no deaths), and one or 2 cases each of rare anomalies. The over-all survival rate in this series was 69%, and of the 13 infants under the age of one month, 9 survived. (An addendum reports a further 20 cases in infants aged less than 12 months, among whom there were 17 survivors, including 7 patients with the tetralogy of Fallot.) The authors conclude that early operation may save the lives of a high proportion of infants with serious cardiovascular malformations.

R. L. Hurt

698. **Isotope Circulation Studies in Congenital Heart Disease**

R. H. GREENSPAN, R. G. LESTER, J. F. MARVIN, and K. AMPLATZ. *Journal of the American Medical Association* [J. Amer. med. Ass.] 169, 667-672, Feb. 14, 1959. 5 figs., 9 refs.

In this paper from the University of Minnesota, Minneapolis, is described a new technique for the detection of intracardiac and extracardiac shunts which obviates the need for femoral arterial puncture. Right-to-left shunts can be accurately detected and located; typical patterns have also been observed in left-to-right shunts and in mitral disease. The procedure involves the injection of trace amounts of a radioisotope into the various chambers of the heart by means of a catheter inserted through a vein. Diagnosis is made from the recordings of appearance times and concentration slopes obtained from two collimated scintillation counters placed respectively over the praecordium and over an extremity. A third counter can be used as desired, either over the lung or over another peripheral vessel.

Sodium and methylglucamine diatrizoate ("renografin") labelled with ^{131}I was used, the dosage being about $1\text{ }\mu\text{c.}$ per kg. of body weight. This was layered in a syringe in front of 5 ml. of saline solution and rapidly injected into the catheter. Second and third injections required doubling and tripling the initial dose to produce enough counts above body background for accurate detection. The material is rapidly excreted when the patient's kidneys are normal and has a biological half-life of less than 5 hours. Radioiodinated serum albumin was initially used in these studies, but was found to have a half-life of 3 days.

The associated equipment was specially designed and consisted of fully transistorized plug-in units. The rate-meters had short-time constants ($\frac{1}{2}$ to 1 second), since information had to be collected over relatively short times, and utilized non-linear scales approximating to a logarithmic 2-octave scale. This was necessary as the short duration of the whole procedure precluded adjustment of the recording parameters, all controls being pre-set, and the recording rates could not be predicted. Permanent recordings were made with a multi-channel recorder.

The procedure demonstrated its usefulness in 42 patients suspected of having right-to-left shunts. The results obtained were characterized by a short interval between appearance of the radioactive material at the heart and its appearance at the femoral artery. Two general groups were observed. In grossly cyanotic patients the early appearance of a large bolus of radioactivity at the femoral artery and a short stay of the material at the heart were observed. This pattern occurred in patients with transposition of the great vessels, cyanotic tetralogy of Fallot, and pseudotruncus. In patients with smaller right-to-left shunts, most frequently septal, there was also early appearance, but the amount of radioactivity appearing early was small and variable, and a shallow slope of appearance was often seen over the femoral artery. Location of the shunt was determined by making multiple injections into various chambers, the most distal chamber or vessel that produced early appearance of radioactivity at the femoral artery being regarded as the site of the right-to-left shunt.

A variety of other conditions were investigated, and a marked delay in the appearance of radioactivity at the femoral artery was among the features noted in 17 patients with disease of the mitral valve. I. M. Rollo

699. Atypical Patent Ductus Arteriosus: the Use of a Vasopressor Agent as a Diagnostic Aid

L. E. CREVASSE and R. B. LOGUE. *Circulation [Circulation]* 19, 332-337, March, 1959. 4 figs., 14 refs.

The murmurs associated with a patent ductus arteriosus (P.D.A.) are variable. In infants, where the pressure gradient between aorta and pulmonary artery is absent or small, there may be no murmur, a systolic pulmonary flow murmur, or a late systolic murmur which continues just past the second sound. As the child grows the pulmonary resistance falls and the systemic pressure rises; there is a large gradient throughout both systole and diastole and the characteristic continuous Gibson

murmur appears. If pulmonary hypertension develops the gradient lessens and only atypical systolic murmurs may remain. When pulmonary and systemic pressures are equal all murmurs may disappear.

The diagnosis of P.D.A. is more difficult in those cases, about 5%, in which the Gibson murmur is absent. The authors, at the Emory University School of Medicine, Georgia, have used the systemic pressor drug mephentermine sulphate to raise the systemic pressure in such cases and thus increase the aorto-pulmonary pressure gradient. By this method they produced the typical continuous murmur in 12 patients with P.D.A. who had atypical murmurs. In each case the diagnosis was confirmed at operation. The drug was given both intramuscularly and intravenously in doses of 10 to 30 mg. according to the age of the patient. It is claimed that the technique is safe and that in some cases cardiac catheterization has been found to be unnecessary.

[This is another example of use of drugs in diagnostic phonocardiography. Barlow and Shillingford (*Brit. Heart J.*, 1958, 20, 162; *Abstr. Wld Med.*, 1958, 24, 268) reported that ejection systolic murmurs can sometimes be distinguished from regurgitant systolic murmurs by a test which involves the inhalation of amyl nitrite.]

D. Emslie-Smith

ARRHYTHMIA

700. Effect of the Cardiac Arrhythmias on the Coronary Circulation

E. CORDAY, H. GOLD, L. B. DE VERA, J. H. WILLIAMS, and J. FIELDS. *Annals of Internal Medicine [Ann. intern. Med.]* 50, 535-553, March, 1959. 10 figs., 33 refs.

In experiments carried out at the Cedars of Lebanon Hospital (University of California School of Medicine), Los Angeles, coronary arterial blood flow was measured in 246 dogs and 4 pigs by the use of the rotameter, the photo-electric dropmeter, and the open-drop method, the coronary sinus flow being measured simultaneously in some cases. The coronary arterial and systemic blood pressures were also measured, and frequently the central venous pressure and cardiac output recorded. The same measurements were then repeated after the development of various arrhythmias, either spontaneous or induced by stroking the heart or by the application of aconitine. In many cases the heart reverted to normal sinus rhythm during the experiment.

The arrhythmias produced were auricular and ventricular extrasystoles, auricular tachycardia, auricular flutter and fibrillation, and ventricular tachycardia and fibrillation. All of these arrhythmias resulted in a significant reduction in coronary arterial flow, particularly if the heart rate was rapid or irregular, and a fall in coronary and systemic blood pressures. The coronary sinus flow varied, but despite this discrepancy it appears clear that arrhythmia reduces the blood supply to the myocardium. Previous work has shown that pressor substances may convert experimental arrhythmias to normal rhythm and it is suggested that this is due, in part at

least, to the correction of the hypotension and the resultant improvement in coronary blood flow. Brachial arterial tracings from human patients showed a similar fall in systemic blood pressure after auricular and ventricular extrasystoles and during auricular fibrillation and flutter with fast ventricular rates. It is argued that these findings indicate that patients with cardiac arrhythmias who exhibit hypotension should be treated promptly with pressor agents, particularly if they have coronary arterial disease. It is also suggested that the difference between "benign" and "malignant" ventricular tachycardia may depend on the degree of hypotension, which was found experimentally to vary with the site of the ectopic focus, even when the ventricular rate was the same.

C. Bruce Perry

CHRONIC VALVULAR DISEASE

701. Pulmonary Function Studies in Patients with Mitral Stenosis

B. L. FRIEDMAN, J. DE J. MACIAS, and P. N. YU. *American Review of Tuberculosis and Pulmonary Diseases* [Amer. Rev. Tuberc.] 79, 265-272, March, 1959. 2 figs., 35 refs.

The authors report from the University of Rochester (New York) School of Medicine a study of the relation between the changes in lung and cardiac function in mitral stenosis. The 69 patients studied were graded clinically according to loss of function into the four categories adopted by the New York Heart Association. In 45 patients (17 males and 28 females ranging in age from 24 to 56 years) studies of lung ventilation (total lung capacity and subdivisions by the helium dilution method; oxygen consumption and minute ventilation during breathing of 100% oxygen; direct maximum breathing capacity; and forced expiratory volume) were related to clinical grading and to haemodynamic data obtained during cardiac catheterization. In the remaining 24 patients (10 males and 14 females aged 24 to 53 years) alveolar and arterial blood gas tensions during the breathing of ambient air and 12% oxygen were related to the haemodynamic data and the clinical grading. In 18 of these patients the diffusing capacity for oxygen and venous admixture were determined by the Riley technique.

Tables of the results are given. The authors found that diminution in vital capacity was closely related to the clinical severity of dyspnoea. There were statistically significant, but materially small, negative correlations between vital capacity and main pulmonary arterial pressure, total pulmonary resistance, and pulmonary vascular resistance; but the maximum breathing capacity was not correlated with haemodynamic findings. The diminished vital capacity was generally associated with an increased residual volume, the total lung capacity remaining approximately normal. In contrast with the results of other workers, this study revealed no consistent increase in the ventilatory equivalent for oxygen in mitral stenosis of increasing severity. The arterial oxygen ten-

sion was markedly decreased in severe mitral stenosis, and there was a corresponding increase in alveolar end-capillary gradient for oxygen, as other workers have reported. In 9 of the 18 cases in which estimations were made the diffusing capacity for oxygen was subnormal, the low values being more frequent in the clinically most severe cases. The authors discuss possible factors causing this reduction in diffusing capacity in mitral stenosis.

P. Hugh-Jones

702. The Role of Vessel Tone in Maintaining Pulmonary Vascular Resistance in Patients with Mitral Stenosis

H. J. SEMLER, J. T. SHEPHERD, and E. H. WOOD. *Circulation* [Circulation] 19, 386-394, March, 1959. 8 figs., 42 refs.

The injection of acetylcholine into the pulmonary artery in doses small enough to be inactivated before reaching the left atrium has been shown to lower the raised pulmonary vascular (arteriolar) resistance (P.V.R.) of mitral stenosis, indicating that it is due in part to increased tone in the smooth muscle of the pulmonary vessels. To examine some of the factors possibly concerned in the maintenance of this tone the P.V.R. was determined at the Mayo Clinic in 58 patients with mitral stenosis 2 to 5 weeks and 8 to 30 months after mitral valvotomy, both at rest and during exercise. Standard methods were used to record data and to calculate flows and resistances. None of the patients had systemic hypertension.

After valvotomy there was a fall in P.V.R. that was directly proportional to the degree of P.V.R. present before operation. The main pulmonary arterial pressure fell more than the pulmonary arterial wedge (left atrial) pressure; hence pulmonary blood flow was maintained by a smaller perfusion pressure. The authors argue that if the pulmonary vessels behaved passively, reduction of the left atrial pressure by valvotomy would tend to raise the P.V.R. by reducing the transmural pressure of the pulmonary vessels and hence the distension of the pulmonary vascular bed. They therefore conclude that the fall in P.V.R. after valvotomy was the result of dilatation of the pulmonary vessels. Since, in dogs, the P.V.R. is low in the presence of pulmonary oedema, this dilatation is probably not due to decreased interstitial oedema, but is the result of active decrease in vessel tone.

In many patients, and especially in those whose resting mean pulmonary arterial pressure was over 30 mm. Hg, the P.V.R. rose during exercise. The main pulmonary arterial pressure rose more than the pulmonary arterial wedge pressure, so that the pressure gradient across the lung rose. The increase in left atrial pressure would tend to distend the vessels, with a consequent fall in resistance, yet in spite of this the P.V.R. rose. Unless this was due to pulmonary oedema, which is unlikely, it was probably the result of active vasoconstriction. The theory is advanced that changes in pressure in the left atrium or pulmonary vascular bed "may be a stimulus capable of regulating tone in the pulmonary vessels of patients with mitral stenosis."

[The authors' closely reasoned arguments do not lend themselves well to abstracting.] D. Emslie-Smith

703. Tricuspid Incompetence following Successful Mitral Valvotomy

P. MOUNSEY. *British Heart Journal* [Brit. Heart J.] 21, 123-129, Jan., 1959. 5 figs., 9 refs.

An uncommon though important complication of mitral valvotomy for mitral stenosis is described. Permanent tricuspid incompetence comes on soon after a successful mitral valvotomy, without any obvious cause for sudden right heart failure, in a patient in whom tricuspid incompetence was absent or only transient or of slight degree. In spite of the development of tricuspid incompetence, the general progress after mitral valvotomy is favourable.

It is suggested that unmasking of a previously latent and minor tricuspid valve lesion as a result of successful mitral valvotomy is the cause of the syndrome, atrial fibrillation being a contributory factor.—[Author's summary.]

CORONARY DISEASE AND MYOCARDIAL INFARCTION

704. The Use of Anticoagulants in Myocardial Infarction. (Лечение больных инфарктом миокарда антикоагулянтами)

B. V. KONJAEV. *Клиническая Медицина* [Klin. Med. (Mosk.)] 37, 81-90, March, 1959. 3 figs., 8 refs.

Of 611 patients with myocardial infarction, 221 (Group A) were treated with anticoagulants (198 with dicoumarol, 19 with "pelentan" (ethyl biscoumacetate) and dicoumarol, and 4 with heparin and dicoumarol) and 390 (Group B) were treated in the orthodox manner without the use of anticoagulants. The indications for anticoagulant therapy were: extensive infarction with circulatory failure and a tendency to aneurysmal dilatation, history or evidence of recent thrombo-embolic phenomena, varicose veins, high serum prothrombin concentration, thrombocytosis, and high serum fibrinogen concentration. Any condition associated with a bleeding tendency was considered a contraindication. The daily dosage of dicoumarol was 200 to 350 mg., of ethyl biscoumacetate 600 to 1,200 mg., and of heparin 50,000 to 67,000 units. In the more serious cases or in the presence of a high initial serum prothrombin concentration a high initial and smaller maintenance dosage was used, whereas when the serum prothrombin concentration was low moderate doses were given for longer periods of time. The mortality was 7.2% in Group A and 10% in Group B. The over-all incidence of thrombo-embolic complications was 10.8% in Group A and 13% in Group B, but the mortality from such complications was the same in the two groups. The incidence of thrombo-embolism in Group A among patients with repeated infarcts was 20%, among those with hypertensive disease 10.3%, and among those with circulatory failure 13.1%, the corresponding figures for Group B being 28%, 14.8%, and 22.2%. The incidence of recurrent infarction was similar in the two groups; of 67 patients in Group A who were given

continuous anticoagulant therapy because of severe angina, 8 developed a second infarct. It was also observed that anticoagulant therapy had no substantial influence on the extension of the infarcts. The incidence of aneurysmal dilatation was 20.8% in Group A and 10% in Group B, but only 18 of the 46 patients in Group A who developed cardiac aneurysm did so during anticoagulant therapy, the dilatation occurring in the remaining cases before treatment started or during a previous episode of infarction. Aneurysm formation seems therefore to be causally related to the severity of the lesion and not to the method of treatment.

During anticoagulant therapy the serum prothrombin concentration was kept, so far as possible, between 40 and 60%, but in 16 of the 24 cases in which thrombo-embolic complications occurred it had risen to between 61 and 66%. It was found that the sudden withdrawal of anticoagulants is liable to result in secondary infarction. It is recommended that treatment should continue until all signs of circulatory embarrassment have disappeared and the function of the myocardium is restored. Transient slight haemorrhages (mainly microscopic haematuria) were observed in 37 cases and severe bleeding (including subarachnoid and petechial subendocardial haemorrhage, haemoptysis, and bleeding from haemorrhoids) in 5 cases. Some patients developed a bleeding tendency while the prothrombin level was relatively high (56 to 76%), and sometimes it actually appeared simultaneously with thrombo-embolic complications. As dicoumarol and its derivatives increase capillary permeability in addition to reducing the serum prothrombin concentration, the simultaneous administration of ascorbic acid and vitamin P is considered advisable.

S. W. Waydenfeld

705. A Clinicopathological Study of Acute Myocardial Infarction and the Role of Anticoagulation Therapy

F. G. CONRAD and N. O. ROTHERMICH. *A.M.A. Archives of Internal Medicine* [A.M.A. Arch. intern. Med.] 103, 421-435, March, 1959. Bibliography.

The records of all patients with unequivocal acute myocardial infarction presenting at the Ohio State University Hospital, Columbus, in the 16 years 1942-57 were reviewed to assess the value of anticoagulant treatment. In the first 8 years (up to 1949) almost no anticoagulants were used, so that this period could serve as a control for the second period when anticoagulants were in general use. After excluding patients who died before adequate clinical evaluation could be made the total of patients left in the study was 623 (441 men and 182 women). The average age of the white men was 59.5 years and of white women 64.6 years, with negro patients a few years younger. The sex ratio for white men and women was 2.2:1 and for negroes 1.1:1. The total mortality was 38% (166 deaths) among the men and 45% (82 deaths) among the women. Diabetes was present in 91 cases (14.5% of the total) and was associated with a higher mortality (60% in men and 52% in women as against 35% and 43% respectively in non-diabetics). A diastolic blood pressure above 95 mm. Hg was found in 169 (38%) of the men and 88 (48%) of the women.

Treatments other than anticoagulation therapy before and after 1950 were comparable, though morphine and sedation were more generously used in the 2nd period. Patients were divided into 3 groups in relation to their anticoagulant treatment. Group 1 (369 patients), received no anticoagulants; of these, 81 (22%) did not receive treatment because they died within 12 hours of admission. Group 2 (108 patients) received inadequate anticoagulant therapy, 11 dying after only one or two doses. In Group 3 (146 patients) depression of prothrombin activity to 30% of normal or less was achieved for 70% of the first 3 weeks after the attack, and therapeutic level was reached within 4 days, this treatment being considered adequate. The mortality was 17.1% in Group 3, 20.4% in Group 2, and 54.5% in the control group. Thrombo-embolic complications developed in 5.5% of the adequately treated group compared with 17.6% in Group 2 and 19.5% in the untreated group. In this connexion it should be pointed out that a number of the thromboses or emboli were found only at necropsy and not clinically, and more patients died and were examined post mortem in the untreated and inadequately treated groups. Of the 146 patients adequately treated, haemorrhage occurred in 5.4% and death due to anticoagulant therapy in 1.4%. Cardiac rupture and haemopericardium were commoner in patients receiving anticoagulants.

The classification of patients as good-risk and poor-risk on admission was not found useful, as a good-risk patient often developed complications later. The mortality of poor-risk patients adequately treated was similar to that of untreated good-risk patients.

It is concluded that all patients should receive anticoagulants immediately after the onset of an acute myocardial infarction.

David Phear

706. The Influence of Anticoagulant Therapy on the Incidence of Thromboembolism, Hemorrhage and Cardiac Rupture in Acute Myocardial Infarction. Correlation of Clinical and Autopsy Data in 100 Cases

N. E. CAPECI and R. L. LEVY. *American Journal of Medicine* [Amer. J. Med.] 26, 76-80, Jan., 1959. 13 refs.

Analysis was made of the clinical records and necropsy reports of 100 patients with acute myocardial infarction who died in the Presbyterian and St. Luke's Hospitals, New York, during the period 1946-53 inclusive. Of these, 50 had received anticoagulant therapy with heparin and dicoumarol and 50 were given comparable general treatment but no anticoagulants. The record of any patient who died during the first 24 hours after admission to hospital was discarded. Complete bed rest was enforced in every instance during the early stages of illness. No case was included in the treated group unless therapy was deemed to have been adequate.

Post-mortem examination had revealed many errors in clinical diagnosis, both with respect to the presence of a recent cardiac infarct and of thrombo-embolic complications. These were found with equal frequency in the treated and the untreated groups, and the incidence was not modified by the presence of congestive heart failure. Major haemorrhage was observed in 6 of the

treated cases, and in 3 of these death was attributed to this cause. The incidence of complications and the accuracy of clinical diagnosis as gauged by findings at necropsy are shown in the following table.

Complication	Not Treated (50 Cases)		Treated (50 Cases)	
	Found at Necropsy	Not Detected Clinically	Found at Necropsy	Not Detected Clinically
Mural thrombi	21 (42%)	16 (76%)	22 (44%)	19 (86%)
Pulmonary emboli	5 (10%)	2 (40%)	6 (12%)	4 (67%)
Systemic emboli	6 (12%)	3 (50%)	9 (18%)	6 (67%)
Major haemorrhage	0	0	6 (12%)	2 (33%)

The incidence of cardiac rupture was small, only one case occurring in the untreated group and 3 cases in the treated group. To give a more satisfactory picture of the comparative incidence of this complication of acute myocardial infarction the authors have combined their series with three other reported series totalling altogether 239 cases treated adequately and 557 untreated cases. In this combined series rupture of the heart was found at necropsy three times as often in the treated (29 cases, or 12.1%) as in the untreated cases (22, or 3.9%). The authors do not claim that these results are suitable for statistical analysis, but only that they seem to demonstrate definite important trends.

T. Semple

707. An Evaluation of Three Revascularization Procedures in the Rehabilitation of the Coronary Patient

A. BLACK and J. E. DELMONICO. *American Journal of Cardiology* [Amer. J. Cardiol.] 3, 68-73, Jan., 1959. 4 figs., 6 refs.

The difficulty of assessing the results of operations designed to revascularize the heart is well known, but the present authors, in the light of their own experience, conclude that surgery has a definite place in the treatment of severe coronary arterial disease. Over the 3-year period 1954-7 three different operative procedures were used in 36 cases. Of 17 patients subjected to cardiopexy with talc, 3 died within 3 months of operation; of the remainder, 13 were alive 1½ to 3 years afterwards. Internal mammary artery ligation was carried out in 15 cases. This relatively minor operation under local anaesthesia was reserved for very bad-risk cases in which thoracotomy and even general anaesthesia were contraindicated. There was one operative death in this group. The Beck I procedure was the operation of choice in 4 patients with advanced symptomatic coronary arterial disease because they were in a younger age group and there were no complications. There was one operative death.

Clinical improvement was noted in 30 of the 36 cases. In half the patients there was complete or almost complete disappearance of angina, and many patients previously completely incapacitated were able to resume their normal occupation. Objective evidence

of improvement in several cases, as seen in electrocardiograms and ballistocardiograms, is presented.

F. J. Sambrook Gowar

HEART FAILURE

708. **Haemodynamic Studies of Cor Pulmonale by the Dye-dilution Method.** (Studio emodinamico del cuore polmonare cronico col metodo della diluizione di colore) L. BINI and L. COLONNA. *Cardiologia pratica* [Cardiol. prat. (Firenze)] 10, 1-36, Feb. [received May], 1959. 51 figs., bibliography.

Working at the Institute of Clinical Medicine of the University of Bari the authors have sought to throw light on some of the physiopathological problems of chronic cor pulmonale by studying the haemodynamics of the condition in 24 patients (18 men, 6 women) in comparison with 10 normal control subjects. They used the dye-dilution technique, an intravenous injection of azovan (Evans) blue being given and serial samples of blood withdrawn from the femoral artery, the concentration of dye being measured spectrophotometrically. The haematocrit value was also determined. From the dye-dilution curves they then calculated the total blood volume, the central blood volume and its fractions—right heart, lungs, and left heart (using the formulae of Newman *et al.* and of Lewis), the cardiac output, and the total peripheral resistance. An estimate was also made of the extent of any short-circuit from the greater to the lesser circulation by way of broncho-pulmonary anastomoses or pleural adhesions by means of the formula of Perosa *et al.* (*Cuore e Circol.*, 1958, 42, 156).

The haematocrit value was high in all but 3 patients, 2 of them women. The central blood volume was generally increased. The right heart blood volume was increased in every patient save one, being sometimes as much as 9 times the normal value. The pulmonary blood volume was increased in all but 5 cases, sometimes by as much as 4 times. The left heart blood volume was increased, though only slightly, in all but 7. In most cases the cardiac output was slightly increased—though in some by as much as 3 times—but in 6 cases it was normal and in 2 diminished. The total peripheral resistance was increased in only 9 patients, all but one of whom were hypertensive and who included 4 of the 6 women in the series. It was shown by calculation from these findings that in a number of cases there was an appreciable transfer of blood from the systemic to the pulmonary circulation. The values for broncho-pulmonary anastomotic flow, cardiac output, pulmonary blood volume, and right heart blood volume tended to show parallel changes, but variations in peripheral haemodynamics were less clearly correlated. In general the symptoms were less marked when haemodynamic abnormalities were small, and vice versa.

The authors suggest that there are two contrasting types of haemodynamic pattern in chronic cor pulmonale. In the first a diminution in the tone and resistance of the pulmonary vascular tree and in cardiac tone results in an increase in central blood volume and a reduction in peripheral volume despite an increase in cardiac output.

In the second type, which is probably less frequent, the pulmonary tone and resistance are maintained, though there is still a slight increase in central blood volume, and cardiac output is normal or diminished, with a definite increase in peripheral blood volume. In both types circulatory symptoms are present, though clearly due to the operation of different mechanisms. The high-output type is characterized clinically by intense cyanosis, venous stasis, a full pulse, and radiological evidence of marked cardiac enlargement and pulmonary engorgement. In the low-output type the state of the right heart is to some extent analogous to that of the left heart in systemic hypertension or to that of the right heart in advanced mitral disease. The haemodynamic picture is not unlike that seen in myocardial or valvular inadequacy. Cyanosis is definite, though not deep, the pulse is small, and there is right ventricular presystolic gallop. With overloading the electrocardiogram shows right-sided preponderance. Radiography shows moderate cardiac enlargement and pulmonary engorgement. The prognosis is more serious in this type of case. The authors claim that this theory covers the observed facts, though the mode of origin of the symptoms of chronic cor pulmonale remains an open question.

A. C. F. Green

709. A Study of Antibiotic Prophylaxis in Patients with Acute Heart Failure

R. G. PETERSDORF and R. K. MERCHANT. *New England Journal of Medicine* [New Engl. J. Med.] 260, 565-575, March 19, 1959. 14 refs.

This paper from the New Haven Hospital (Yale University School of Medicine), Connecticut, reports an attempted clinical appraisal of the practice of administering a broad-spectrum antibiotic as a prophylactic measure during acute episodes of cardiac decompensation. A double-blind trial was carried out on 150 patients admitted in acute heart failure, those with obvious infections and those dying within 48 hours being excluded. One group of 72 patients received 2 g. of chloramphenicol daily for 7 days, while the remaining 78 received an identical placebo. The two groups were chosen at random and were comparable in respect of sex, age, race, and aetiology and severity of cardiac disease. Hypertension, coronary arterial disease, valvular disease, and cor pulmonale accounted for most of the episodes of failure. A total of 38 patients died during the study, 21 in the antibiotic group and 17 in the placebo group. Pneumonia was found in 10 of the 35 patients examined post mortem, 7 of them being in the treated group and 3 in the placebo group. Of 4 other patients who developed clinical evidence of pulmonary infection, one was receiving chloramphenicol.

The authors conclude that although pulmonary congestion and infection may be closely related, the prophylactic administration of antibiotics will not prevent the development of pneumonia in patients with heart failure. This is best recognized by the presence of purulent sputum and confirmed radiologically, and it is good practice to treat this pulmonary infection vigorously only as it arises, and with the appropriate antibiotic.

T. Semple

Clinical Haematology

710. Thrombocytopenia and Hypocalcemia. A New Method for Their Production in Dogs and an Evaluation of Their Significance in Abnormal Bleeding

H. S. WINCHELL, S. GOLLUB, E. EHRLICH, and A. W. ULIN. *Surgery [Surgery]* 45, 357-365, March, 1959. 7 figs., 26 refs.

The role of the blood platelets in the production of abnormal bleeding is not fully understood, and in particular, although "haemorrhage following massive transfusion" is probably related to a variety of postoperative factors rather than to the transfusion, much remains to be done before the importance of the various components which may be involved in clotting can be assessed. The present study was undertaken at Hahnemann Medical College, Philadelphia, to clarify the role of a low platelet count combined with a low calcium level alone in the production of abnormal bleeding, these deficiencies being produced in dogs by means of an extra-corporeal shunt from femoral artery to vein through a system containing a cation exchange resin. Although platelet counts as low as 23,000 per c. mm. and calcium levels as low as 4.3 mg. per 100 ml. were produced, no evidence of abnormal bleeding was noted.

The authors conclude from their findings that neither of these factors can be the sole cause of a haemorrhagic diathesis.

A. Brown

711. Thrombocytopenia in Massive Transfusion. Mechanism of Production and Evaluation of Role in Producing Abnormal Bleeding

S. GOLLUB, H. S. WINCHELL, E. EHRLICH, and A. ULIN. *Surgery [Surgery]* 45, 366-370, March, 1959. 14 refs.

A study of the literature on the effects of massive transfusion has revealed that some doubt exists as to the incidence and importance of thrombocytopenia after such treatment. This further paper [see Abstract 710] reports an investigation of changes in the platelet count in 41 patients undergoing surgery and receiving transfusions of 2.6 to 13.5 litres of blood in the first 2 hours after operation.

In most of the patients who showed a postoperative abnormal bleeding tendency thrombocytopenia was observed; however, an almost identical degree of thrombocytopenia was found in patients who received similar volumes of blood, but in whom haemorrhage was not excessive.

The authors conclude that it is clear that simple thrombocytopenia alone was not the cause of the bleeding tendency when it did develop, although it may have been a contributory factor. They suggest that the thrombocytopenia may, however, have been at least in part related to the transfusion, as for example by dilution of the patient's blood with platelet-poor banked blood.

A. Brown

712. Neurologic Complications of Leukemias and Lymphomas

W. E. HUNT, B. A. BOURONCLE, and J. N. MEAGHER. *Journal of Neurosurgery [J. Neurosurg.]* 16, 135-151, March [received May], 1959. 7 figs., 19 refs.

After a brief survey of the literature on the neurological complications of leukaemia, lymphosarcoma, and Hodgkin's disease the authors describe their own experience of 1,264 cases seen at the Ohio State University Hospital, Columbus, during the 3 years 1954-7.

Among 815 cases of leukaemia of all types the most frequent neurological complications were due to intracerebral, subarachnoid, or intraspinal haemorrhage associated with thrombocytopenia; in this type of complication, from which 86 patients died, the authors consider there is no place for surgical treatment. In contrast, however, 15 of the patients with leukaemia had other forms of neurological involvement which were amenable to treatment. These fell into three groups: (1) The "pseudo-tumour" or "hydrops" type, with increased intracranial pressure secondary to meningeal and perivascular infiltration; this was the most common type and affected 11 patients, in whom a good response was achieved by x-irradiation usually combined with chemotherapy, which by itself was relatively ineffective in treating this complication. (2) Hydrocephalus of communicating type occurred in one patient and was uninfluenced by x-ray treatment; however, as the leukaemia was reasonably well controlled a shunting operation was performed and gave marked relief. (3) The remaining 3 patients suffered from perineural and intra-axial infiltration causing multiple cranial nerve palsies, peripheral neuropathies, or signs of intra-axial destructive lesions. In the authors' experience these patients respond less consistently to x-ray therapy and the prognosis in such cases is worse.

The neurological complications of Hodgkin's disease, of which there were 257 cases in this series, were less clear-cut. In 3 patients the complications were associated with thrombocytopenic haemorrhage, but 13 had neurological complications due to a granuloma invading or compressing the nervous system, either in the form of extradural compression of the spinal cord or as an intracerebral tumour. There was also a group with more doubtful neurological complications in which the possibility of torulosis or post-irradiation myelopathy could not be completely ruled out. Lymphosarcoma produced both the above types of neurological complication, that is, either a pseudo-tumour picture or compression symptoms due to a lymphosarcomatous mass behaving like the granuloma of Hodgkin's disease. For both the latter disease and lymphosarcoma, when the site of the lesion can be located, the treatment of choice is x-ray therapy combined with chemotherapy; mustine (nitrogen mustard) is also effective in the control of extra-

dural granuloma. In the more obscure neurological syndromes associated with Hodgkin's disease the response to other methods of treatment has been only moderate. The authors particularly warn against the danger of treating a post-irradiation myelopathy with further x-ray therapy, a pitfall often overlooked since this neurological sequel may not manifest itself until 3 years or more after the original course of irradiation.

J. B. Stanton

713. Adult Leukaemia. Trends in Mortality in Relation to Aetiology

W. M. C. BROWN and R. DOLL. *British Medical Journal* [Brit. med. J.] 1, 1063-1069, April 25, 1959. 12 refs.

The death rates from leukaemia in males in 5-year age groups from age 15 in England and Wales in the three periods, 1945-9, 1950-4, and 1955-7 are first tabulated for each of 9 diagnostic subgroups. After certain assumptions have been made about deaths for which full information about clinical and cytological type was not available on the death certificate, estimated death rates for the same periods and age groups are then tabulated for chronic lymphatic leukaemia, chronic myeloid leukaemia, and acute leukaemia, and the analysis is mainly concerned with these three types. Deaths attributed to plasma-cell leukaemia were not included as it was considered that they ought to be classified with multiple myeloma.

Between 1945-9 and 1955-7 the male mortality from leukaemia of all types increased, the relative increase being greater after age 60 than before that age. Above age 60 each of the three types contributed to the increased mortality, whereas at younger ages the increase was largely due to acute leukaemia. The authors show that in 1955-7 mortality estimated to be due to chronic lymphatic leukaemia increased with age from age 30 (0.3 per million) to age 80 years (137.6 per million) roughly in proportion to the sixth power of the age. In the same period the estimated mortality from chronic myeloid leukaemia increased from age 15 (0.7 per million) to age 80 years (59.5 per million) roughly in proportion to the third power of the age. The association between age and estimated mortality from acute leukaemia in 1955-7 is rather different; the rate fell from 28.2 per million at age 15-19 years to a minimum of 17.5 per million at 25-29 years, then increasing slowly to 20.8 per million at 35-39 years and more rapidly thereafter to a maximum of 104.6 per million at age 70-74 years. The increase after age 45 was approximately in proportion to age to the power of 2.5. Similar age-specific mortality rates are tabulated for women for the three types of leukaemia, and these show similar time and age trends, although the recent increases among women have been slightly less than among men. Thus in 1955-7 the estimated mortality rates per million women were: for chronic lymphatic leukaemia, 0.3 at age 35-39 and 57.6 at 75-79; for chronic myeloid leukaemia, 1.3 at age 15-19 and 35.6 at 80 and over; and for acute leukaemia, 17.0 at age 15-19 and 14.9, 20.5, and 18.5 respectively in the next three age groups, the rate increasing thereafter to 159.2 per million at 75-79 years. At most ages the sex ratio (male:female)

of mortality had a fairly distinct value for each type of leukaemia; thus in 1955-7 the crude ratio was 2:1 for chronic lymphatic leukaemia, 1.2:1 for chronic myeloid leukaemia, and 1.4:1 for acute leukaemia.

The authors discuss the possible sources of error in these data and consider whether the increases in the reported rates reflect true increases in the incidence of the disease. After a well reasoned argument they conclude that the causes of the three types of leukaemia are different, although they suggest that chronic myeloid and acute leukaemia might have a common cause acting through different mechanisms. In arriving at these conclusions they draw attention to (1) the distinctive differences in the sex ratios of the three types, (2) the similarity of the association between age and mortality from chronic lymphatic leukaemia and that between age and mortality from most epithelial tumours, the associations between age and mortality from other types of leukaemia being in sharp contrast; and (3) the one major difference between acute and chronic myeloid leukaemia, namely, that mortality from the acute type is relatively high in adolescence (and even higher in childhood) and then falls until about the age of 30 before it begins to rise again.

The final conclusion is that the principal characteristic of the real increase in leukaemia is a change in the incidence of the acute type, which is compatible with the theory that increased exposure to ionizing radiation has played some part in the rise in incidence of the disease.

E. A. Cheeseman

714. Leukemia and Medical Radiation

D. W. POLHEMUS and R. KOCH. *Pediatrics* [Pediatrics] 23, 453-461, March, 1959. 2 figs., 23 refs.

The authors report the results of a comparison of the radiation history, obtained in most cases by postal inquiry, of 251 out of 317 children with leukaemia seen at the Children's Hospital, Los Angeles, during the period 1950-7 with that of an equal number of matched controls. It was found that of the 251 leukaemic patients, of whom 56% were males and 44% females, 172 (69%) had been exposed to some type of radiation compared with 48% of the controls, a difference which is statistically highly significant. A single diagnostic x-ray examination was the source of radiation in most cases, 135 of the patients having been so exposed compared with 104 controls. Fluoroscopy of the chest or alimentary tract had been carried out on 17 (6.8%) of the leukaemic group compared with 8 (3.2%) of the controls, this difference being suggestive, but not highly significant. Antenatal diagnostic radiography of the mother was rather more frequent in the leukaemic group (75 cases) than in the control group (58), but this difference is not regarded as significant. The clearest difference was apparent between the children who had received deep irradiation of cervical lymph nodes or of the thymus gland and those who had not—thus 12 (4.8%) of the leukaemic children had been so treated, compared with 2 (0.8%) of the controls. In this group males predominated in the ratio of 6:1, but the reason for this sex difference is not clear.

J. L. Markson

Respiratory System

715. Long-Term Treatment of Bronchiectasis and Chronic Bronchitis: a Controlled Study of the Effects of Tetracycline, Penicillin, and an Oleandomycin-Penicillin Mixture

N. S. CHERNIACK, K. L. VOSTI, H. F. DOWLING, M. H. LEPPER, and G. G. JACKSON. *A.M.A. Archives of Internal Medicine* [A.M.A. Arch. intern. Med.] 103, 345-353, March, 1959. 14 refs.

A double-blind study to evaluate long-term oral treatment with antibiotics in controlling the pulmonary infections that may occur in bronchiectasis and chronic bronchitis is reported from the University of Illinois College of Medicine, Chicago. Patients with a history of chronic productive cough for one year or more with repeated lower respiratory tract infections were regarded as suffering from bronchiectasis if bronchography showed one or more areas of bronchiectasis, whereas those in whom no area of bronchiectasis could be demonstrated by bronchography were considered to have chronic bronchitis. Of the 67 patients included in the study, 45 were regarded as having bronchiectasis and 14 chronic bronchitis; in the remaining 8 cases the diagnosis was undetermined. Treatment was continued for 3 to 22 months and consisted in: (1) 2 g. of tetracycline (17 patients); (2) 1 g. (1,600,000 units) of potassium benzylpenicillin (17 patients); (3) 2 g. of a combination of oleandomycin (1.3 g.) and penicillin (0.7 g.) (16 patients); or (4) sucrose (17 patients)—each daily in 4 doses. Before treatment the chest was radiographed, a complete blood count performed, and serum total protein and C-reacting protein levels and protein electrophoretic patterns determined. Hypogammaglobulinaemic patients discovered in this way numbered 4, one in each group. Sputum samples were homogenized in sterile physiological saline solution and a sputum flake from each sample was washed 3 times in saline solution. Cultures from each of these preparations were prepared on (1) human fresh-blood agar; (2) blood agar containing 1 unit of penicillin per ml.; (3) eosin-methylene-blue agar; and (4) Sabouraud's agar. The two fresh-blood media were streaked with a staphylococcus to facilitate recognition of *Haemophilus influenzae*. Duplicate cultures were made on all media except Sabouraud's; one set was incubated aerobically and the other under CO₂ tension. Sabouraud cultures were incubated aerobically. Pulmonary function tests were carried out before treatment and again one year later. The four treatment groups were comparable in all respects.

Patients treated with tetracycline suffered significantly fewer infections of the lower respiratory tract than those given penicillin or the placebo, and the average duration of such episodes was shorter. Patients treated with oleandomycin-penicillin were ill for a significantly lower number of days than either the control or the penicillin-treated group. The results in the group treated

with penicillin alone were no better in this respect than those in the control group. Tetracycline treatment significantly reduced the frequency with which pneumococci and coagulase-positive staphylococci were isolated from the sputum; this applied also to *H. influenzae*, but not to a statistically significant degree. Treatment with oleandomycin-penicillin reduced only the frequency of isolation of coagulase-positive staphylococci. Patients from whom *H. influenzae* was isolated suffered more days of lower respiratory tract infections than patients from whom this organism had never been isolated.

K. Zinnemann

716. The Relation between Consumption of Tobacco and Mortality from Malignant Tumours of the Lungs in Italy. (Sui rapporti fra consumo di tabacco e mortalità per tumori maligni del polmone in Italia)

G. AGNESE. *Igiene moderna* [Igiene mod.] 51, 801-820, Nov.-Dec., 1958 [received May, 1959]. 3 figs., 17 refs.

The author, working at the University of Genoa, has investigated the relationship between tobacco smoking and mortality from lung cancer in the various regions and provinces of Italy. A considerable correlation ($r=0.751$) was found between the lung cancer mortality in the 19 regions in the years 1952-4 and the consumption of tobacco in those regions in 1953-4. An even more significant correlation ($r=0.779$) was observed between the mortality in 1953-4 and the amount of tobacco consumed during the period 1927-54 in the 88 provinces. Further analysis showed that the highest correlation was obtained when the consumption of cigarettes alone was considered ($r=0.887$; $P<0.01$); no correlation was observed between mortality from lung cancer and the consumption of cigars or pipe tobacco.

The recent increase in mortality from lung cancer in Italy has been accompanied by an increase in cigarette smoking; consumption of tobacco in other forms has diminished during the same period.

A. J. Karlish

717. The Relation between Mortality from Malignant Tumours of the Lung and Certain Suspected Causative Factors. (Sui rapporti fra mortalità per tumori maligni del polmone in Italia ed alcuni sospetti fattori favorenti)

G. AGNESE. *Igiene moderna* [Igiene mod.] 51, 821-844, Nov.-Dec., 1958 [received May, 1959]. 13 refs.

In this further study from the University of Genoa the mortality rate for lung cancer in the various Italian provinces is related to: (1) cigarette smoking; (2) the number of motor vehicles registered for taxation per kilometre of roads; (3) degree of industrialization (as indicated by the proportion of the population employed in industry); (4) average winter temperature; and (5) mortality from malignant tumours of other sites.

Cigarette smoking was found to be the factor most significantly correlated with mortality from lung cancer.

Even allowing for the possible concomitant influences of the other factors considered, a clearly significant partial regression was observed between lung cancer mortality and cigarette consumption per head of population ($P < 0.01$). Regional data showed a moderate but significant partial regression ($P = 0.01$ to 0.05) between lung cancer mortality and the number of motor vehicles and the degree of industrialization in so far as this concerned the metallurgical, engineering, and chemical industries.

A. J. Karlish

718. The Statistical Investigation of Smoking and Cancer of the Lung

J. BERKSON. *Proceedings of the Staff Meetings of the Mayo Clinic* [Proc. Mayo Clin.] **34**, 206-224a, April 15, 1959. 4 figs., 39 refs.

The author reviews critically the statistical evidence in support of the theory that tobacco smoking is an important cause of cancer of the lung. In particular he considers the prospective studies of Doll and Hill (*Brit. med. J.*, 1954, **1**, 1451, and 1956, **2**, 1071; *Abstr. Wld Med.*, 1954, **16**, 418, and 1957, **21**, 404), and of Hammond and Horn (*J. Amer. med. Ass.*, 1958, **166**, 1159 and 1294; *Abstr. Wld Med.*, 1958, **24**, 308 and 309), and he uses data from these reports to show that the association between smoking and mortality rates exists not only for cancer of the lung but also for other causes of death. He states that this general association is also apparent in the preliminary results of a similar study, as yet unpublished, relating to United States veterans with insurance policies registered with the Veterans Bureau. Consequently he suggests that it is more reasonable to seek a single explanation of the association between smoking and disease in general than separate explanations of associations between smoking and particular diseases.

Three such explanations are offered for consideration. The first is that the observed associations result from a "spurious statistical phenomenon". In support of this the reliability of smoking histories and certification of cause of death is questioned and it is asserted that in none of the investigations referred to above were the samples studied "an adequately large proportion of the reference population". The second possible explanation is that constitutional differences between smokers and non-smokers account for the association, and this implies that persons who smoke little or not at all are constitutionally disposed to longevity and that their disposition not to smoke is a reflection of this constitution. Studies are quoted in support of this explanation, notably those of Fisher (*Nature (Lond.)*, 1958, **182**, 108 and 596) in which a comparison of the smoking habits of monozygotic and dizygotic twins suggested a genetic difference between smokers and non-smokers. [In so far as cancer of the lung is concerned, various aspects of these explanations have been considered in the reports of the original prospective studies, particularly those of Doll and Hill.]

The third possible explanation is based on the concept of "rate of living" put forward by Pearl some 30 years ago. It is suggested that smoking may accelerate the rate of living and that smokers of a given chrono-

logical age group may thus experience the increasing death rates of non-smokers of an older chronological age group. In other words, smokers may age biologically more rapidly than non-smokers. The author suggests that experiments on animals might well be undertaken to observe the results of exposure to inhalation of tobacco smoke, not only in terms of the production of local bronchogenic effects, but also in terms of generalized effects.

E. A. Cheeseman

719. Survival in Lung Cancer

K. R. BOUCOT, U. HORIE, and M. J. SOKOLOFF. *New England Journal of Medicine* [New Engl. J. Med.] **260**, 742-746, April 9, 1959. 4 figs., 17 refs.

A follow-up study is reported of 250 consecutive cases of primary lung cancer seen at two chest x-ray clinics in Philadelphia between 1947 and 1957. Official surveys in Philadelphia have shown that, contrary to the experience of some other workers, the incidence of cancer of the lung is twice as high in negroes as it is in white subjects.

The over-all 5-year survival rate in the present series was 17%. Exploration was carried out in 133 of the cases and resection in 73, the 5-year survival rate in the resected group being 37%. In patients over 55 the 5-year survival rate was higher (20%) than in those under 55 (12%). There were too few females in the series for a valid comparison of the survival rates in the two sexes to be made. The survival rate was higher in patients with squamous-celled carcinoma than in those with adenocarcinoma or undifferentiated growths. The prognosis was better in patients in whom the lesions presented as solitary nodules on x-ray examination than in those with lesions other than solitary nodules.

It is suggested that measures to detect early cases of lung cancer should include biennial "x-ray examinations of the chest of asymptomatic older persons and exhaustive clinical study of persons in the cancer age group who have respiratory symptoms". John Fry

720. The Natural History of Carcinoma of the Lung

G. L. EMERSON, M. S. EMERSON, and C. E. SHERWOOD. *Journal of Thoracic Surgery* [J. thorac. Surg.] **37**, 291-304, March, 1959. 15 figs., 5 refs.

In this study of 360 proved cases of carcinoma of the lung reported from the Departments of Medicine, Radiology, and Surgery of the University of Rochester, New York, data in respect of age, sex, occupation, and smoking habits of the patients, together with duration of symptoms, survival time, and other relevant findings are presented in a series of 11 tables [without comment], while the radiographic appearances are classified and illustrated.

Delay in diagnosis is discussed. The average delay between the first symptoms and clinical diagnosis was 7 months and that between early radiographic change and diagnosis was 4 months. It is suggested that this may have been due in part to the fact that in some mass radiological surveys the films are frequently read by physicians who are neither radiologists nor chest specialists.

B. Golberg

Urogenital System

721. Estimation of Severity of the Nephrotic Syndrome in Childhood as a Guide to Therapy and Prognosis

W. W. McGRORY, M. RAPOPORT, and D. S. FLEISHER. *Pediatrics* [*Pediatrics*] 23, 861-873, May, 1959. 5 figs., 20 refs.

This paper from the University of Pennsylvania, Philadelphia, reports an attempt to assess the prognosis of the nephrotic syndrome based on findings in 20 children with this condition. Although patients with haematuria, raised blood non-protein nitrogen level, and/or hypertension tend to do badly, the difference between different groups graded on this basis was not impressive. The severity of the glomerular "leak" of albumin was estimated by calculating the clearance of albumin (C_A) in relation to the creatinine clearance (C_{Cr}). Patients with a high glomerular permeability to albumin as judged by the $C_A:C_{Cr}$ ratio tended to show a poor response to steroid therapy. Further, it appeared that the response to steroid therapy itself provided a good index of the severity of the disease and of the ultimate prognosis. In the small group studied it appeared that long-term therapeutic effects were much better in those given steroid therapy aimed not so much at controlling oedema as at inducing maximum improvement. In the former, steroids were given for 10 to 14 days to induce diuresis and repeated if oedema recurred in the latter they were given for 28 days, and in cases showing persistent activity of the renal lesion maintenance therapy was given for 4 consecutive days weekly. A follow-up of 80 similar patients treated with the former regimen showed that 43 (55%) were oedema-free 4 years later, whereas 80% of 37 patients given the longer treatment were oedema-free after 3 years.

C. Bruce Perry

722. Treatment of the Nephrotic Syndrome with Triamcinolone

L. HELLMAN, B. ZUMOFF, A. MINSKY, N. KRETCHMER, and B. KRAMER. *Pediatrics* [*Pediatrics*] 23, 686-689, April, 1959. 7 refs.

Triamcinolone, a new synthetic steroid, was tried in the treatment of the nephrotic syndrome in 15 children, aged 1 to 9 years, at New York Hospital-Cornell Medical Center and Maimonides Hospital, New York. Usually the drug was given in a dosage of 20 mg. daily by mouth until all the findings on analysis of the blood and urine were normal or, if no improvement occurred, for 6 weeks. The clinical data and the results are set out in a table. In 10 of the children there was complete remission (defined as induction of a satisfactory diuresis with return of the blood and urine to normal) and in 4 partial remission; in one patient the treatment failed. The typical response to triamcinolone was an abrupt

diuresis beginning 10 to 12 days after the start of treatment and resulting in the disappearance of all retained fluid in the next 3 to 4 days. No systematic changes were observed in the serum concentration of sodium or potassium, and the urinary excretion of protein decreased rapidly. There were no psychic changes and no side-effects except for slight moon face in a few patients. Of the 10 patients who obtained a complete remission, 5 subsequently relapsed within 1 to 4 months; 3 of these responded to a second course of triamcinolone with a further complete remission, while one obtained partial remission.

The results of this study indicate that triamcinolone is a highly effective therapeutic agent in the control of acute remission of the nephrotic syndrome in children. They compare favourably with reported results obtained with other steroids.

J. M. Smellie

723. The Use of Chlorothiazide in the Nephrotic Syndrome

G. E. BURCH and H. A. WHITE. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] 103, 369-380, March, 1959. 9 figs., 19 refs.

Chlorothiazide has been widely used to promote diuresis in heart failure, cirrhosis, and the nephrotic syndrome. At the Charity Hospital, New Orleans, it was given to 10 patients with the nephrotic syndrome, 5 of whom had chronic glomerulonephritis, 4 the Kimmelstiel-Wilson syndrome, and one amyloid disease secondary to chronic osteomyelitis. A dosage of 0.5 g. twice a day produced a good diuresis in all 10 patients, the drug generally being much more effective than mercurial diuretics. In all the patients there was increased excretion of sodium and chloride with little increase in potassium excretion. The percentage increases in excretion of electrolytes during administration of chlorothiazide compared with the control periods were 64 for sodium, 59 for chloride, and 28 for potassium. The rates of plasma clearance of electrolytes were increased, but no change was observed in creatinine clearance, which indicated that the glomerular filtration rate was unchanged.

Chlorothiazide had no effect on blood pressure in the 4 normotensive patients and the 4 with mild hypertension (140/90 to 155/100 mm. Hg), but in one of the 2 patients with severe hypertension, who was also receiving reserpine, the blood pressure fell on administration of chlorothiazide. In 8 patients all oedema subsided; in the remaining 2 there was only the facial oedema associated with steroid therapy.

A maintenance dose of 0.25 g. of chlorothiazide daily was effective in preventing oedema, even in patients with low serum protein and albumin levels.

David Phear

Endocrinology

724. A Study of Endocrine Function in 29 Cases of Anorexia Nervosa and Functional Wasting in Young Women. (Étude des fonctions hormonales dans 29 cas d'anorexie mentale et de maigreur fonctionnelle des jeunes filles)

M. ALBEAUX-FERNET, J. CHABOT, and M. GELINET. *Semaine des hôpitaux de Paris* [Sem. Hôp. Paris] 35, 1000-1003, March 18, 1959. 4 figs., 8 refs.

At the Hôpital Laënnec and the Institut National d'Hygiène, Paris, the case records of 60 young women with anorexia nervosa or functional loss of weight were studied, and those of 29 who had been adequately investigated endocrinologically selected for analysis. Of these 29, 22 had amenorrhoea, in 20 of whom it dated from the onset of the disorder. In the 2 cases in which amenorrhoea came on later it was attributed to malnutrition. In general the periods did not return until some time after the weight had returned to normal. The return of the periods or the development of overweight was taken as a definite indication that the condition was cured. Urinary excretion of follicular stimulating hormone was found to be low in only 2 or 3 cases in the series. There was no evidence of pituitary insufficiency.

A. G. Mullins

725. Status of the Thyroid Gland after Age 50

T. H. MCGAVACK and W. SEEGER. *Metabolism: Clinical and Experimental* [Metabolism] 8, 136-150, March, 1959. 7 figs., 32 refs.

The authors describe from New York Medical College a study of thyroid function in older persons in which 610 inmates of a chronic disease hospital and of a home for the aged (501 being over 60) were examined. In each decade after the age of 50 there was a decrease in the proportion of normal-sized glands, as estimated by palpation, and an increase in that of "small" glands (that is, under 20 g. in estimated weight). The basal metabolic rate, determined in 22% of the subjects, showed a steady decline with increasing age, though there was a tendency not to decrease further after the age of 80. The serum cholesterol level varied widely, ranging from 95 to 397 mg. per 100 ml. The 24-hour thyroid uptake of radioactive iodine (^{131}I) in 429 subjects aged 60 to 101 was compared with that in a control group of subjects aged 25 to 40; this showed that a sharp decline in the average uptake of ^{131}I occurs in the age group 40 to 59, and that this reduction is maintained in those over 59. The uptake for men was slightly higher than that for women, except in those over the age of 90. The uptake of ^{131}I in response to a single 5-unit dose of thyroid-stimulating hormone was determined in 20 subjects aged over 65 and found to be normal in 16. In 54 subjects in whom the serum protein-bound iodine level was estimated no correlation with age was observed. Of 37 women

with clinically recognizable thyroid disease, 35% (13 subjects) had disorders of the genital tract compared with only 7% of those with a clinically normal thyroid gland. The thyroid disorders noted in this series included non-toxic nodular goitre (21 cases), hyperthyroidism (6), hypothyroidism (2), diffuse non-toxic goitre (6), and carcinoma of the gland (2).

J. N. Agate

726. A Clinical Study of Parathyroid Tetany. (Опыт клинического изучения паратиреопривных тетаний) G. M. GUREVIČ. *Проблемы Эндокринологии и Гормонотерапии* [Probl. Endokr. Gormonoter.] 5, 52-57, March-April, 1959. 5 refs.

Among 745 patients treated surgically for thyroid disease during the period 1950-7 at the author's clinic in Kharkov the total incidence of postoperative tetany was 0.6% (5 patients) and in thyrotoxic cases 1.1%. In his opinion accidental removal of the parathyroid glands in the course of subtotal thyroidectomy is not the chief cause of postoperative tetany, since with modern methods this is very unlikely to occur. He considers that most of these cases are due to traumatic stretching of the nerves supplying the glands or to interference with their blood supply by scar tissue. In some cases in which there is evidence of hypothyroidism after the operation the administration of thyroxine or thyroid extract will prevent or at least diminish the attacks of tetany. In one of his cases they ceased after a dense scar in the neck, adherent to the subjacent tissue, had been softened and mobilized by physiotherapy; in others blood transfusions allayed the attacks; and in yet another the subcutaneous implantation of thyroid tissue from a patient with thyrotoxicosis relieved the tetany permanently. Two cases are cited in which emotional disturbances precipitated the attacks.

Postoperative parathyroid insufficiency may be temporary or chronic, 4 cases in the present series being of the former and one (together with 2 others treated by the author after operation elsewhere) of the latter type. After careful evaluation of each case treatment was started with a blood transfusion (125 to 250 ml.) followed by 5 to 10 ml. of 10% calcium chloride solution intravenously, after which 15 ml. of the same solution was given 3 times a day by mouth. A strict milk diet was given, with the addition of powdered egg-shell in farina and vitamin D. While the blood calcium level is often reduced in postoperative tetany, it must be borne in mind that attacks can occur with a normal blood calcium level, which is therefore not a reliable guide to progress. Return to normal diet must be cautious, as the products of protein fermentation in the bowel may be absorbed into the blood stream and cause a recurrence of symptoms, necessitating a return to milk diet. Thyroid implantation often has a remarkable effect, but this may be only temporary.

L. Firman-Edwards

DIABETES MELLITUS

727. Pancreatic Action of the Sulfonylureas

A. R. COLWELL and J. A. COLWELL. *Journal of Laboratory and Clinical Medicine* [J. Lab. clin. Med.] 53, 376-395, March, 1959. 9 figs., bibliography.

A series of experiments on dogs, designed to demonstrate the site or sites of the hypoglycaemic action of the sulphonylurea compounds, were carried out at the Northwestern University Medical School, Chicago. Solutions containing tolbutamide or, in a few cases, carbutamide were infused for 20 minutes into the pancreatic artery, the femoral vein, the hepatic artery, or the portal vein of the animals. The femoral venous blood sugar levels during the subsequent 4 hours were compared with those in dogs receiving control solutions. In all the animals there was an increase in the blood glucose level as a result of the anaesthesia and of the surgical procedure necessary for cannulation of the particular vessel.

Infusion of sulphonylurea into the pancreatic artery in a dose of 7 mg. per kg. body weight, producing a concentration in the femoral vein which preliminary tests suggested would not itself be associated with a fall in blood sugar level, resulted in a sustained hypoglycaemia. Infusion of similar solutions into the femoral vein and the hepatic artery produced only slight falls in the blood sugar level compared with the pre-anaesthetic levels. No significant fall occurred after infusion into the portal vein. In none of the experiments did control infusions produce hypoglycaemia. In 4 animals tolbutamide was infused into the pancreatic artery 6 months after the pancreatic duct had been ligated. Some hypoglycaemic response was still apparent.

In summary, these experiments showed that the injection of a small amount of tolbutamide into the pancreas induced hypoglycaemia, whereas the same amount introduced into the liver or into a peripheral vein failed to do so. The authors conclude that this is further evidence favouring the pancreas as the primary site of action of the sulphonylurea compounds. They suggest that these drugs provoke a slow and slight but sustained discharge of insulin from the pancreatic islets, with a resulting reduction in hepatic glucose output and in the peripheral venous blood sugar level.

H.-J. B. Galbraith

728. Clinical Evaluation of Formamidinyliminourae, a New Biguanide Oral Blood Sugar Lowering Compound: Comparison with Other Hypoglycemic Agents

L. P. KRALL and R. F. BRADLEY. *Annals of Internal Medicine* [Ann. intern. Med.] 50, 586-613, March, 1959. 8 figs., bibliography.

The effectiveness of the diguanides in lowering the blood sugar level was evaluated in 173 diabetic patients at the Joslin Clinic and New England Deaconess Hospital, Boston, Massachusetts. Four diguanide compounds—the phenethyl, the normal amyl, the *iso*amyl, and the methylbenzyl derivatives of formamidinyliminourae—were used, administration being by mouth. The patients ranged in age from 4 to 80 years, and the

duration of diabetes was from less than one year to 35 years (average 9.8 years); 31 patients had had no insulin before the trial, and the remainder had been having from 5 to 136 units of insulin daily. All patients were receiving weighed diabetic diets. Response to the drugs was judged by changes in blood and urinary sugar levels. The result was considered to be satisfactory if in patients not taking insulin the blood sugar level fell by at least 25%, and in the remaining patients when the insulin could be entirely replaced by the diguanides or the dose reduced by at least half. In most cases a placebo was also occasionally substituted during treatment.

A satisfactory reduction in blood sugar level was obtained in 150 cases (88%), but in 43 of these the diguanide had to be discontinued because of side-effects. In the 107 "successful" cases the total daily dose of diguanide was 50 to 450 mg. Side-effects usually appeared at daily dosages of 200 to 300 mg., varying with the different compounds, and were mainly gastro-intestinal. No significant alterations in the results of liver or renal function tests or in blood count were observed. The duration of diabetes appeared to be the most important factor relating to success—the shorter the duration, the better the result. Higher daily insulin requirement was also associated with a lower success rate, whereas age was not a significant factor.

The action of other oral hypoglycaemic agents is reviewed, particularly "synthalin" (dodecamethylene-diguanidine), but also "neosynthalin", myrtillin, carbutamide, and tolbutamide. The main advantage of the diguanides over these other drugs lies in the absence of toxic effects after their administration.

The authors conclude that the diguanides control the blood sugar level satisfactorily in mild or moderate diabetes, either when given alone or with insulin, and are well tolerated. They do, however, lack other beneficial metabolic effects of insulin, and are unsuitable in severe diabetes, in which they are also less well tolerated. The long-term evaluation of the diguanides is at present uncertain and awaits further clinical trial.

Gerald Sandler

729. The Insulin Equivalence of Salicylate

J. REID and T. D. LIGHTBODY. *British Medical Journal* [Brit. med. J.] 1, 897-900, April 4, 1959. 4 figs., 6 refs.

The antidiabetic effect of aspirin previously reported (Reid *et al.*, *Brit. med. J.*, 1957, 2, 1071; *Abstr. Wld Med.*, 1958, 23, 453) has been further investigated by the authors at the Western Infirmary, Glasgow. To 14 diabetic out-patients under treatment with insulin zinc suspension (I.Z.S.) aspirin was given in doses, averaging 20 grains (1.3 g.) 5 times daily, high enough to produce a serum salicylate level of 35 to 45 mg. per 100 ml. Eight of the patients, whose initial requirement of I.Z.S. was 12 to 48 units daily, were able to do without insulin altogether while aspirin was being administered. In another 5 cases the insulin requirement, initially 22 to 76 units daily, was reduced by 10 to 20 units, but to judge from the lability of the fasting blood sugar level in these patients both with insulin alone and with insulin and aspirin their diabetes was not well controlled by either form of treatment. In the remaining case an insulin requirement

of 112 units was reduced by 72 units; the fasting blood sugar level was stable both with and without aspirin, but was about half as high during aspirin treatment, indicating an insulin equivalence of more than 72 units. Many patients exhibited toxic effects from aspirin overdosage, especially at the beginning of the experiment.

It is concluded that aspirin has a definite antidiabetic effect, and that further studies are justified to try to overcome the undesirable side-effects of salicylate therapy and to find out how it acts.

A. I. Suchett-Kaye

ADRENAL GLANDS

730. The Inhibitory Effect of Triamcinolone on Adrenal Function

C. B. HATFIELD and S. SHUSTER. *Journal of Clinical Pathology* [J. clin. Path.] 12, 140-142, March, 1959. 1 fig., 11 refs.

Inhibition of the secretion of hydrocortisone, which is normally caused by injection of certain steroid hormones, has proved a useful means of demonstrating an intact pituitary-adrenal axis, and in some cases helps to distinguish between adrenal cortical neoplasia and hyperplasia. A disadvantage of the technique is that many of the steroids, when given in suppressive doses, contribute significantly to the metabolites whose concentration in the urine and plasma is used as an index of adrenal activity.

In this paper from the Postgraduate Medical School of London a study is reported of the ability of triamcinolone to depress the secretion of hydrocortisone by the adrenal cortex in a healthy male aged 31 years and in a girl aged 16 years with cirrhosis of the liver without ascites. The urinary excretion of corticosteroids and the plasma hydrocortisone level were estimated for a control period of 2 days. The subjects were then given 8 mg. of triamcinolone 4 times a day for 5 and 11 days respectively and the urinary excretion of steroids and the plasma hydrocortisone level again determined at intervals. Triamcinolone caused marked depression of hydrocortisone secretion and did not produce a significant amount of plasma or urinary chromogen. ACTH (corticotrophin) gel, given while the subjects were still receiving triamcinolone, immediately restored hydrocortisone secretion, indicating that the drug does not act directly on the adrenal cortex. Toxic effects of the steroid necessitated cessation of a trial in one additional subject.

P. A. Nasmyth

731. Adrenocortical Function in Obesity. (Les fonctions cortico-surrénales dans l'obésité)

M. ALBEAUX-FERNET, J. CHABOT, and J. D. ROMANI. *Semaine des hôpitaux de Paris* [Sem. Hôp. Paris] 35, 993-1000, March 18, 1959. 1 fig., 28 refs.

This paper from the Hôpital Laennec and the Institut National d'Hygiène, Paris, describes a study of adrenocortical function in 53 women with obesity, none of whom were manifestly suffering from Cushing's disease. In most cases the excretion of 17-ketosteroids, like that of 17-hydroxysteroids, was abnormally low or at the lower limit of normal, though low readings for 17-

hydroxysteroids occurred more constantly than low readings for 17-ketosteroids. This partial adrenal insufficiency was considered to be purely functional, due to confinement to bed and restrictions of hospital life.

The excretion of aldosterone was studied in 5 cases while the subjects were given successively a normal sodium intake, a moderately low-sodium diet, and a high-sodium diet. In 2 cases the subjects were then given a very low sodium intake (200 mg. daily) and in one a high sodium intake (6 g. daily). The amount of aldosterone excreted and its variation with the amount of sodium in the diet were within normal limits. It is concluded that the amount of extracellular fluid in the obese is normal and that the excess fluid and sodium in such cases are held in the interstitial spaces. In the obese subject given a high sodium intake the excess was not eliminated, so that there was a marked rise in weight although in other respects the diet remained restricted. In this sense obesity is comparable to oedema with salt retention. In 2 cases the excretion of aldosterone was studied at different points in the menstrual cycle. There was frank hyperaldosteronism during the second half of the cycle, comparable with the hyperaldosteronism that has been observed in obese women during periods of gain in weight.

A. G. Mullins

732. The Adrenal Cortex in Itsenko-Cushing's Disease. (Кора надпочечников при болезни Иценко-Кушинга)

E. I. TARAKANOV and T. A. ŠEITKOVA. *Проблемы Эндокринологии и Гормонотерапии* [Probl. Endokr. Gormonoter.] 5, 58-63, March-April, 1959. 24 refs.

The authors have studied the morphological and histochemical changes in the cells of the adrenal cortex in 4 cases of Cushing's syndrome. Three of the specimens were taken from glands totally or partially resected at operation and one from a patient who died of pneumonia in a late stage of the disease.

The hypertrophy and hyperplasia of the adrenal cortex found in this disease are due to the excessive production of corticotrophin by the pituitary gland as a result of the poor output of hydrocortisone. The effect of this is to produce an intensive synthesis and secretion of androgens such as 4-androsterone, androstenedione, and 11-hydroxyandrostenedione. Two stages of hypertrophy were observed: (1) accumulation of lipids in the cells (initially in the zona glomerulosa) and increased secretion of corticosteroids, particularly of glucocorticoids; and later (2) reduction of lipids and perverted biosynthesis of steroid hormones, with increase in the neutral 17-ketosteroids and decrease in oestrogens. The two stages can be distinguished histochemically.

The authors advocate large doses of cortisone or hydrocortisone in the treatment of the disease to suppress the reaction of the pituitary and the consequent excessive production of virilizing and neutral steroids. They consider that resection of the adrenal glands is justifiable only in the first stage of cortical hypertrophy. The article is illustrated by 5 photomicrographs reproduced in colour. [This is unusual in a Russian publication.—EDITOR.]

L. Firman-Edwards

The Rheumatic Diseases

733. "Rheumatic" Iritis and Iridocyclitis

F. LENOCH, V. KRÁLÍK, and J. BARTOŠ. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 18, 45-48, March, 1959. 6 refs.

The authors of this paper from the Research Institute for Rheumatic Diseases and the First Ophthalmological Clinic, Prague, state that they have never seen iritis and iridocyclitis in acute rheumatic fever and only rarely in rheumatoid arthritis. They have, however, seen these ocular lesions fairly frequently in ankylosing spondylitis, and they have reviewed the records of 625 cases (570 in males and 55 in females) of this disease for evidence of these complications. This revealed definite uveal affection in 163 of the males and 16 of the females—an over-all percentage of 28.9. They then examined 474 patients (269 male and 205 female) who were attending the ophthalmological clinic with iritis or iridocyclitis of obscure aetiology. Among these they found 91 patients (83 males and 8 females) with ankylosing spondylitis, the age distribution being very similar to that in the cases of ankylosing spondylitis previously reviewed. They conclude that a high proportion of patients with ankylosing spondylitis have iritis, and recommend that in all cases of iritis of unknown aetiology a careful search for ankylosing spondylitis should be made.

B. M. Ansell

734. Histological, Histochemical and Electron Microscopic Observations on Synovial Membrane

J. D. LEVER and E. H. R. FORD. *Anatomical Record* [Anat. Rec.] 132, 525-539, Dec., 1958 [received June, 1959]. 9 figs., 19 refs.

Biopsy specimens of synovial membrane from joints of rabbits, cats, and man were examined histochemically and by light and electron microscopy at the Anatomy School of the University of Cambridge. While some parts of the synovium showed an absence of lining cells, in other situations these were several layers thick. The cytoplasm of the synovial cells, as well as the intercellular material, was deeply stained by the periodic-acid-Schiff method, and this reaction was not abolished by previous exposure to hyaluronidase. [Such abolition was not to be expected.] A metachromatic reaction was shown only by granules in a few deeply situated cells, assumed to be mast cells. Under the electron microscope the cells of the synovial surface were shown to contain dense, granular bodies 0.05 to 0.16 μ in diameter. Some of these cells had a degenerate appearance.

The authors consider that it is these surface cells and the cells immediately subjacent rather than the cells of the deeper layers or the mast cells which produce synovial mucin. The positive periodic-acid-Schiff reaction is presumed to be due to the hyaluric acid of the joint fluid. [The suggestion of Asboe-Hansen (*Ann. rheum. Dis.*, 1950, 9, 149) that hyaluric acid is derived from mast-

cell heparin is in any case most unlikely owing to the great chemical differences between these two acid polysaccharides.]

G. Loewi

735. The Problem of Interrelation between Diffuse Generalized Scleroderma, Acrosclerosis, Raynaud's Phenomenon and Raynaud's Disease. [In English]

Z. ŠTÁVA. *Dermatologica* [Dermatologica (Basel)] 118, 1-11, Jan. [received March], 1959. 10 refs.

The author reviews a series of 70 patients with diffuse scleroderma who were followed up for periods of 8 to 10 years at the Second Dermatological Clinic of Charles University, Prague. Raynaud's phenomenon was present in 60 patients (57 women, 3 men), its onset having preceded the onset of the scleroderma (by 2 to 34 years) in 41 cases and developed simultaneously with it in 19. It appeared that the earlier Raynaud's phenomenon develops and the shorter the interval between its onset and that of scleroderma, the worse the prognosis. In 5 cases rheumatoid arthritis of the hands preceded Raynaud's phenomenon and in 14 cases the onset of rheumatoid arthritis and scleroderma coincided. All these cases proved to be serious, with rapid progression.

The author considers that "there is a very close relation between Raynaud's disease and scleroderma of the acrosclerotic type to the point of possibly being the same disease with different degrees of involvement".

I. McLean Baird

CHRONIC RHEUMATISM

736. Reiter's Disease in the Female

J. K. OATES and G. W. CSONKA. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 18, 37-44, March, 1959. 3 figs., 19 refs.

Reiter's disease may be associated with bacillary dysentery, non-specific diarrhoea, or a venereally acquired infection, although the dysenteric syndrome is apparently rare in Great Britain. With the growing interest in this disease numerous reports have appeared, and all authorities agree that the venereal syndrome rarely affects the female. The present report deals with 14 cases in females seen in London—10 from the White-chapel Clinic and 4 from a total of 213 cases of Reiter's syndrome seen at St. Mary's Hospital over the past 15 years. Two patients had 2 attacks and the remainder a single attack. The age of onset varied between 18 and 58 years, and only one patient was coloured. In 7 attacks there was proved gonococcal infection and in 3 presumptive evidence of gonorrhoea, while the remaining 6 attacks were of the "non-specific" variety. The general pattern of the disease, and the x-ray changes were similar to those seen in males, with the possible exception that monarticular cases were more frequent (5). In the 10 instances thought to have been due

to gonococcal infection treatment was with penicillin, but in only one case did the arthritis improve after this therapy. In 2 cases the course of the disease was prolonged—6 and 10 years; in 3 it lasted approximately 2 years and in the remainder it cleared within 8 months.

While the present report confirms that Reiter's syndrome is uncommon in the female, it also suggests that the possibility of misdiagnosis is probably greater in women than in men. In all the cases described it was preceded by genital infection, but not every attack of infection was followed by arthritis. There was no apparent reason for this, nor was it possible to suggest why this syndrome is more common in the male than in the female.

B. M. Ansell

737. A Study of Reiter's Syndrome Based on 80 Cases Observed in Tunisia. (Le syndrome de Fiessinger-Leroy-Reiter; enseignements fournis par l'étude de 80 cas observés en Tunisie)

A. MASBERNARD. *Revue du rhumatisme et des maladies ostéo-articulaires* [Rev. Rhum.] 26, 21-45, Jan. [received May], 1959. 1 fig., 36 refs.

The author reports 80 cases of post-dysenteric Reiter's syndrome occurring in military personnel in Tunisia. The incidence of the syndrome followed closely the incidence of dysentery from June to December and affected mainly young men who had arrived recently from France. Urethritis, mostly abacterial in nature, was present in 80%, eye involvement in 94%, and arthritis in 96% of cases. The arthritis affected mostly the lower limbs, especially the knees. In the more severe cases marked muscular wasting, particularly of the quadriceps femoris, became one of the most intractable features of the syndrome. In 4 cases there were transient cardiac murmurs with abnormal electrocardiographic findings. There was a well marked increase in the α_2 -globulin fraction of the serum proteins in no less than 94% of cases; a rise in the γ -globulin level was found in 60% of cases.

Aureomycin appeared to prevent later complications such as ankylosing spondylitis if given early; once the syndrome was well established, however, antibiotics proved ineffective. Diacetylpyrocatechol given in combination with prednisone was found to be the most effective treatment for the established condition.

G. W. Csonka

738. Ankylosing Spondylitis in Women

F. D. HART and K. C. ROBINSON. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 18, 15-23, March, 1959. 6 figs., 8 refs.

Some clinical and radiological features of 30 female patients with ankylosing spondylitis are described. This disease appears to run a milder course in women than in men, but a very variable rate of development is noted. Radiological abnormalities in the symphysis pubis were frequently seen. Bilateral lesions of the hip joints developed rapidly in 2 patients, and were the cause of severe disability; both had been treated by immobilization and this is regarded as having been responsible for the subsequent fixation of these joints. Pregnancy and

childbirth had little effect on the course of the disease. The value of phenylbutazone for the relief of symptoms is stressed.—[Authors' summary.]

739. Serum Responses in Rheumatoid Arthritis. [Review Article]

J. H. VAUGHAN. *American Journal of Medicine* [Amer. J. Med.] 26, 596-613, April, 1959. 4 figs., bibliography.

740. A Comparison of the Latex Fixation-Whole Serum, Latex Fixation-Euglobulin Fraction and Bentonite Flocculation Tests in the Laboratory Diagnosis of Rheumatoid Arthritis

H. L. HOLLEY, A. ULLOA, M. HENRY, S. GRIFFIN, and M. L. JOHNSTON. *American Journal of the Medical Sciences* [Amer. J. med. Sci.] 237, 345-351, March, 1959.

Several serological tests have been described in recent years as aids in the diagnosis of rheumatoid arthritis; all are based on the presence in the serum of a protein of high molecular weight associated with the γ -globulin fraction and known as the "rheumatoid factor". In this study, carried out at the Veterans Administration Hospital, Birmingham, Alabama, the authors have compared three such tests, namely, the latex fixation test using whole serum as described by Singer and Plotz, the latex fixation test using the euglobulin fraction as described by Craig, Kerby, and Persons (*J. Lab. clin. Med.*, 1957, 49, 635), and the bentonite flocculation test of Bozicevich *et al.* (*Proc. Soc. exp. Biol. (N.Y.)*, 1958, 97, 180; *Abstr. Wld Med.*, 1958, 24, 212). Each test was performed on sera from (1) 76 patients aged 19 to 72 with a clinical diagnosis of rheumatoid arthritis (fulfilling the criteria of the American Rheumatism Association (A.R.A.) apart from the finding of a positive agglutination reaction); (2) 9 patients with "atypical rheumatoid arthritis", that is, with a disease clinically suggestive of rheumatoid arthritis but not fulfilling the criteria of the A.R.A.; and (3) 71 patients with musculoskeletal disease other than rheumatoid arthritis, these being divided into 11 separate diagnostic categories.

The whole-serum latex fixation method gave a positive result in 56 (74%) of the 76 patients in Group 1. A difference in the results obtained between the two sexes was noted, 81% of the men but only 69% of the women giving a positive reaction, suggesting perhaps that a separate disease mimicking rheumatoid arthritis may occur in middle-aged women. None of the patients in Group 2 and only one in Group 3 (a patient with systemic lupus erythematosus) gave a positive result with this test.

The latex fixation test using euglobulin gave a positive result in 86% of the 76 patients in Group 1, a negative result in all in Group 2, while in Group 3 only 2 patients (one with systemic lupus erythematosus and one with Sjögren's syndrome) gave a positive reaction. Lastly, with the bentonite flocculation test a positive result was obtained in 88% of cases in Group 1, in none in Group 2, and in only 4 cases (2 of systemic lupus erythematosus and 2 of the "shoulder-hand syndrome") in Group 3.

The authors state that those patients with definite rheumatoid arthritis who showed no agglutinating acti-

vity by any of the 3 tests are being subjected to a latex inhibition test which may reduce the size of this group. The significance of the reactions is discussed and the present results compared with those of other workers. It is of interest that in this series all three tests of agglutinating activity were negative in patients with osteoarthritis, ankylosing spondylitis, gout, Reiter's syndrome, Still's disease, scleroderma, "infectious arthritis", and rheumatic fever.

I. Berkinshaw-Smith

741. Significance of the Waaler-Rose Test, Streptococcal Agglutination, and Antistreptolysin Titre in the Prognosis of Rheumatoid Arthritis

H. A. OTTEN and F. W. BOERMA. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 18, 24-28, March, 1959. 15 refs.

In this paper from the University of Groningen the authors report a study of the course of rheumatoid arthritis in 141 patients seen in the initial stage of the disease and followed up for 1 to 3 years. In 106 cases (Group A) the duration of the disease at the time of the first examination was 1 to 3 months, while in 35 (Group B) it was 4 to 6 months. Of the 106 patients in Group A, 37 gave a positive reaction to the Waaler-Rose test, and at the end of the first year 11 of these had recovered compared with 49 (out of 69) giving a negative reaction. Increased antistreptolysin titres were observed more often in the seronegative group than in the seropositive group or in healthy subjects. A positive response to streptococcal agglutination tests was obtained in 28 of the 37 seropositive patients compared with only 8 of the 69 seronegative.

The authors state that the early stages of rheumatoid arthritis were seen as frequently in males as in females, but after 3 years joint involvement was found in nearly three times as many women (16) as in men (6). Arthritis of the finger joints seemed to be of little prognostic value. In the first year of observation some 57% of patients in Group A and 31% of those in Group B recovered. After the first year recovery was rare, whatever the result of the Waaler-Rose test.

K. C. Robinson

742. Response to Serotonin and Its Antagonists in Patients with Rheumatoid Arthritis and Related Diseases

A. L. SCHERBEL and J. W. HARRISON. *Angiology* [Angiology] 10, 29-33, Feb., 1959. 2 figs., 8 refs.

At the Cleveland Clinic Foundation, Ohio, the local response to injection of serotonin in 23 patients with rheumatoid arthritis was compared with that in 16 healthy controls. In the patients only uninvolved joints were injected. The dosage of serotonin was 0.01 mg. intra-articularly into the proximal interphalangeal joints of the fingers, 0.05 or 0.1 mg. periarticularly near a proximal finger joint, and 0.1 mg. intradermally on the back of the hand. Diffuse painful oedema and erythema with cyanosis, sometimes spreading over the back of the hand and the wrist and lasting 1 to 2 hours or more, developed in 20 of the patients, but in only one of the controls. Antagonists to serotonin given intravenously abolished the cyanosis in 10 minutes. Similar results were obtained in 15 patients with systemic lupus

erythematosus or scleroderma. It is concluded that patients with rheumatoid arthritis and related disorders are less able to inhibit serotonin than are healthy subjects.

J. A. Cosh

743. Effect of Intramuscular Injection of Pituitary Tissue in Rheumatoid Arthritis

P. FORGÁCS, L. BAKOS, G. CSASZAR, and E. RIESZ. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 18, 34-36, March, 1959. 16 refs.

The efficacy of intramuscular injections of pituitary tissue in the treatment of rheumatoid arthritis was studied at the National Institute for Balneological Research, Budapest, 20 patients being given the following injections at weekly intervals over a period of 4 weeks: (1) 20 units of long-acting corticotrophin (ACTH); (2) calf pituitary tissue; (3) a saline placebo; and (4) brain tissue homogenate. The clinical response and the urinary excretion of 17-ketosteroids were observed. The pituitary implant failed to produce any greater improvement than the control injection, which in turn was less effective than ACTH. There was little or no adrenal response to any of the injections.

K. C. Robinson

744. Indications for Surgical Intervention in Rheumatoid Arthritis of the Wrist and Hand

J. C. F. CREGAN. *Annals of the Rheumatic Diseases* [Ann. rheum. Dis.] 18, 29-33, March, 1959. 12 refs.

Various operations have been performed on the wrist and hand to relieve pain and disability due to rheumatoid arthritis. The author reviews some of these with reference to the results obtained in 71 patients operated on out of a total of 290 polyarthritic patients seen over a 6-year period at hospitals in the South Manchester area and the Devonshire Royal Hospital, Buxton. In the wrist the results of excision of the lower end of the ulna (sometimes combined with arthrodesis of the wrist) and of excision of the flexor tendon sheath were good. The results of simple excision of the distal end of the ulna were variable, but were best when 2½ inches (6.35 cm.) of this bone were removed. Inability to make use of the thumb was one of the greatest single disabling factors. Two main types of disability of the thumb were seen—instability of the metacarpo-phalangeal joint, in which arthrodesis of the joint was successful, and fixed deformity of the whole thumb in a bad position. In the latter group resection of the proximal third of the first metacarpal was unsuccessful unless absorbable gauze was introduced between the bone surfaces. Extensor tendon ruptures were repaired by direct suture or tendon transfer in 13 cases, but the deformity soon recurred in 8. The results of tendon transfer were better than those of direct suture. In the fingers excision of the second and fifth metacarpal heads and necks relieved pain and produced a better grasp, but the results of arthroplasty of the interphalangeal joints were poor.

In the author's view the indications for surgery in these patients are limited, since the existing deformity is often compatible with reasonable function.

Peter Ring

Neurology and Neurosurgery

745. Neurologic and Electroencephalographic Studies in Open Heart Surgery. A Preliminary Report

F. TORRES, G. S. FRANK, M. M. COHEN, C. W. LILLEHEI, and N. KASPAR. *Neurology* [*Neurology (Minneapolis)*] 9, 174-183, March, 1959. 4 figs., 9 refs.

The neurological and electroencephalographic (EEG) abnormalities associated with congenital heart disease were studied at the University of Minnesota Hospitals, Minneapolis, in 32 patients chosen at random from 101 who were subjected to cardiac surgery by the extracorporeal circulation technique. In 11 of the 32 patients the EEG was abnormal and neurological signs were present before operation. In 27 the EEG was recorded during operation. The authors summarize their findings as follows.

"In most of the patients who showed electrical abnormality (73%), this was predominant in posterior temporal, parietal, and occipital regions. The surgical procedure in most cases only temporarily affected the EEG record and the clinical neurologic picture. In 2 control patients having anesthesia and uncomplicated intrathoracic operations without perfusion, postoperative EEGs were temporarily more abnormal than their preoperative tracings.

It is suggested that congenital alteration of cerebral blood supply secondary to heart disease produces disturbances which prevent the normal maturation of electrical rhythms. This is manifested in adults by EEG abnormalities that resemble those frequently seen in children. Future correlation of neurologic and EEG findings with pathologic studies of the central nervous system will probably greatly contribute to the study of origin and development of cerebral electrical activity."

J. MacD. Holmes

746. Effects of Delayed Anticoagulant Therapy on Experimental Cerebral Infarcts

A. F. PETERMAN, K. G. WAKIM, G. P. SAYRE, J. P. WHISNANT, and C. H. MILLIKAN. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] 18, 263-269, April, 1959. 2 figs., 11 refs.

Experiments were carried out at the Mayo Clinic to determine the influence of anticoagulants upon the evolution of induced cerebral infarction in dogs. In 52 animals infarction was produced by the intracarotid injection of small quantities of the animal's own blood which had clotted and been allowed to stand for 48 hours. After 3 days approximately half of the animals were given dicoumarol, and over the following 9 to 15 days the prothrombin levels were maintained at a mean of 25% below the normal. Gross and microscopical examination of the infarctions at the end of this period showed that there was no difference between the treated and untreated groups as regards size or state of develop-

ment of the infarction. On the other hand there was conspicuously more haemorrhage in the infarctions in the treated animals, and the mortality in this group was higher than in the control group. J. B. Cavanagh

747. Anticoagulants for Occlusive Cerebrovascular Lesions

E. F. VASTOLA and A. FRUGH. *Neurology* [*Neurology (Minneapolis)*] 9, 143-148, March, 1959. 7 refs.

There is considerable evidence to suggest that anticoagulants modify favourably the natural course of the syndromes of basilar and carotid artery insufficiency. At Kings County Hospital, New York City, anticoagulants were given to 55 patients in whom there was a presumptive clinical diagnosis of a recent occlusive cerebrovascular lesion. None of the patients was more than slightly hypertensive, and none showed evidence of haemorrhage on lumbar puncture. As regards progression of an incomplete lesion and the rate and degree of recovery the clinical course was no more favourable in the patients given anticoagulants than that expected in a similar group treated only by supportive measures. In 20 of the 55 patients haemorrhage occurred in various parts of the body during treatment. The authors do not consider that this high incidence is related simply to the degree of prothrombin depression; other factors, such as haematuria associated with cystitis or the "injudicious use" of catheters, play a part.

In 4 patients anticoagulants were responsible for extensive haemorrhage into the brain; in 3 of these haemorrhage occurred in the region involved by the initial occlusive lesion and in the fourth bleeding occurred in a different region. It is suggested that the true incidence of this complication was probably higher, since in most cases there was no adequate search for haemorrhage. Of the 55 patients, 16 died during the period of the study, 28 improved, and 11 showed no change in response to treatment.

The authors conclude that the risk of intracerebral haemorrhage "appears to contraindicate the use of anticoagulants in the treatment of cerebral vascular occlusion under the conditions described".

J. MacD. Holmes

748. Cognitive Changes following Temporal Lobectomy for Relief of Temporal Lobe Epilepsy

V. MEYER. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] 81, 299-309, March, 1959. 26 refs.

At the Institute of Psychiatry (Maudsley Hospital), London, the author has investigated the long-term effects of temporal lobectomy on intellectual function in 25 epileptic patients who formed part of a series previously described by Falconer *et al.* (*Lancet*, 1955, 1, 827; *Abstr. Wld Med.*, 1955, 18, 320). These had been tested

before and again one month after operation, and 17 of them have now been re-examined by a number of intelligence tests one year after operation. It was found that operation on the non-dominant side had not materially affected the general intelligence or learning ability. Operation on the dominant side, however, resulted in impairment of certain specific abilities, especially that of auditory verbal learning, but left practically unaffected general intelligence and visual and tactile learning ability.

The tests used were the Wechsler-Bellevue, Mill Hill Vocabulary, Progressive Matrices, and New Word Learning and Retention tests, together with 6 learning tests dealing with auditory-verbal recall, auditory-verbal recognition, visual-verbal recognition, visual-design recognition, visual-design recall, and tactile-design recognition.

G. de M. Rudolf

749. Psychological Factors Involved in Bizarre Seizures. Report of Four Cases

M. E. CHAFETZ and R. S. SCHWAB. *Psychosomatic Medicine [Psychosom. Med.]* 21, 96-105, March-April, 1959. 3 figs., 15 refs.

The authors report that during the past 6 years 20 patients with atypical epileptic seizures have been seen at the Children's Medical Center or Massachusetts General Hospital, Boston. They point out that these cases represent a borderland problem in which the neurological abnormality is accompanied by a significant psychological disturbance, leading to special difficulty in diagnosis and treatment. Four representative case histories are described in detail. In this group of patients the seizures tended to occur in clusters and thereafter the patients often remained symptom-free for some time. It was observed that psychological stress was frequently associated with an increased incidence of seizures. Owing to the bizarre nature of many of the seizures, as well as the presence of severe emotional difficulty, psychiatric consultation became essential.

They have found that a collaborative approach, involving a neurologist and a psychiatrist, offers the most effective means of treatment, since they consider that the separation of the roles of neurologist and psychiatrist is desirable in order that the patient may not exploit his physical needs in order to block psychological exploration. It is suggested that the capricious and atypical seizure pattern may be explained by the fact that unresolved emotional conflicts lead to a lowering of the seizure threshold. In their view the use of the term hysteroid epilepsy is undesirable, and the diagnostician should not hesitate to describe the two separate entities, namely, epilepsy and personality disorder.

A. Balfour Sclaire

750. Bilateral Retrobulbar Optic Neuritis

R. HIERONS and T. K. LYLE. *Brain [Brain]* 82, 56-67, March, 1959. 36 refs.

The literature relating to patients whose presenting affection was bilateral retrobulbar neuritis is reviewed. The clinical data of 47 personally observed cases of bilateral retrobulbar neuritis are summarized together

with details of their course. These patients have been followed up for 2 to 15 years, the average follow-up period being 6 years in the case of the adults and 4½ years in the children.

The adult cases have been classified into the following clinical groups: (1) Those in which both eyes were involved simultaneously or in which the second eye was affected within a few days of the first, loss of vision occurring rapidly and reaching a maximum in less than a week. In approximately half of these cases vision improved or recovered. Neurological features were observed in some but no patient, as yet, has developed characteristic symptoms or signs of disseminated sclerosis. (2) Those in which both eyes were involved simultaneously with gradual deterioration of vision over a period of up to 6 months. A good recovery occurred in about half of these cases. One patient had neurological signs and another an increased cell count of the C.S.F. (3) and (4) Those in which an interval of several months or years elapsed before the second eye was involved. These cases showed the highest percentage of recovery of vision (about three quarters). Some 40% of these patients had neurological signs. (5) A small group (2 cases only) with recurrent attacks in both eyes. Both patients are well 8 years later. No reference has been found in the literature to this type of case.

Details of 13 cases in children are described in which visual recovery was on the whole, particularly good. One patient only in this group has developed signs of disseminated sclerosis.

It is suggested that a localized form of encephalomyelitis is responsible for many of the cases in childhood and perhaps for some of the adult cases. In 8 of the adult cases it is likely that disseminated sclerosis is the cause of the condition, and it is possible that in others this may eventually prove to be the diagnosis. In some cases in spite of the negative family history Leber's optic atrophy may be the appropriate diagnostic label.

It is hoped that we shall be able to follow up most of these 47 cases and report upon them again at a later date.—[Authors' summary.]

751. The Cervical Spinal Canal in Syringomyelia

C. E. C. WELLS, J. D. SPILLANE, and A. S. BLIGH. *Brain [Brain]* 82, 23-40, March, 1959. 14 figs., 25 refs.

The diameter of the cervical spinal canal in syringomyelia was studied in standard lateral radiographs obtained in 32 cases referred to the Department of Neurology, Cardiff Royal Infirmary. Preliminary examination of radiographs of the spinal canal in 30 healthy subjects had confirmed the findings of Wolf *et al.* (*J. Mt Sinai Hosp.*, 1956, 23, 283) that the average diameter in normal subjects is 22 mm. at C 1, 20 mm. at C 2, and 17 mm. from C 3 to C 7 inclusive.

Of the 32 patients in the present series, 17 were under 30 years of age at the time of onset of syringomyelia and 15 were over 30. In 14 of the former group and one of the latter the spinal canal was abnormally wide. Apart from age at onset of the disease there were no features distinguishing the patients with an abnormally wide canal from the others.

In a long and detailed discussion the authors state that the absence of erosion in pedicles and laminae rules out pressure atrophy of the vertebrae from the expanding cord as a cause of the widening. The observation that the vertebrae were normal in shape suggested that the syringomyelia and the wide canal are not due to a common disorder of growth, while the finding of a wide cervical canal mainly in cases of early onset indicates that the neural arches adapt themselves during growth to the abnormal size of the cervical cord.

N. S. Alcock

752. Cerebrospinal-fluid Culture in Multiple Sclerosis

H. MAVOR, F. W. GALLAGHER, and G. A. SCHUMACHER. *New England Journal of Medicine* [New Engl. J. Med.] 260, 860-863, April 23, 1959. 8 refs.

In an attempt to isolate the spirochaete reported by Ichelson (*Proc. Soc. exp. Biol.* (N.Y.), 1957, 95, 57; *Abstr. Wld Med.*, 1958, 23, 5) to be recoverable from the cerebrospinal fluid (C.S.F.) in 78% of cases of disseminated (multiple) sclerosis the authors cultured C.S.F. from 12 clinically undoubted examples of this disease and 14 control cases of other (mainly neurological) diseases. Particular care was taken to follow Ichelson's technique as closely as possible. It was found impossible, however, to sterilize the culture medium as recommended by filtration through an unglazed porcelain filter (Selas 03), the pores of which were quickly blocked by the agar component. The medium was therefore first filtered through paper, then through a diatomaceous earth (Mandler) filter, and finally through the fine Selas filter. As most of the agar was thus removed from the medium the authors question the appropriateness of this method of sterilization, since the presence of agar is presumably important in fostering anaerobiosis.

The 26 specimens of C.S.F. obtained were incubated anaerobically in this medium at 30° C. for at least 30 days and examined by dark-field illumination before being discarded. Six tubes were contaminated with Gram-positive bacilli or cocci. No positive cultures were obtained from any of the remaining 20 specimens (9 from patients with disseminated sclerosis, 11 from control subjects).

J. B. Cavanagh

753. Search for a Neuromuscular Blocking Agent in the Blood of Patients with Myasthenia Gravis

W. L. NASTUK, A. J. L. STRAUSS, and K. E. OSSERMAN. *American Journal of Medicine* [Amer. J. Med.] 26, 394-409, March, 1959. 4 figs., 13 refs.

Specimens of plasma and serum from 22 patients with myasthenia gravis at Mount Sinai Hospital, New York, were tested for the possible presence of an agent which inhibits neuromuscular transmission, similar specimens from 9 healthy subjects serving as controls. Some of the specimens were taken after exercise under ischaemia. The effects of various dilutions of the samples on the indirectly excited maximal twitch and tetanic tensions of the sciatic-nerve-sartorius muscle of the frog were studied *in vitro*. Specimens from only 5 of the myasthenic patients caused some reduction in maximal tetanic tension beyond that produced by control

specimens. Indeed, samples from 13 of the myasthenic patients and from 3 of the controls actually caused an appreciable augmentation of the sartorius-muscle contractions. [Direct stimulation of the muscle was not employed, and there is no clear evidence indicating whether the effects described were due to an action upon neuromuscular transmission or to an action upon the muscle fibre itself.] The paper includes a useful discussion of the difficulties and limitations of such methods of analysis, but the results obtained neither support nor rule out the possibility that myasthenia gravis is associated with a circulating neuromuscular blocking agent.

W. C. Bowman

754. Determination of the Electrical Resistance of the Skin as a Means of Studying the Functional Recovery of the Sympathetic Supply after Surgical Interruption. (La résistance électrique cutanée en tant que moyen de contrôle de la reprise fonctionnelle du sympathique après interruption chirurgicale)

W. MONTORSI, C. GHIRINGHELLI, G. TIBERIO, and F. LAVORATO. *Presse médicale* [Presse méd.] 67, 508-510, March 14, 1959. 6 figs., bibliography.

The authors, writing from the General Surgical Clinic, University of Milan, comment on the many theories advanced to explain the regaining of autonomic function in the limbs which follows interruption of the sympathetic nerve supply. In view of the interest in this subject they review their own experiences with one method of assessing autonomic function, namely, measurement of skin resistance. The apparatus employed was a modification of that of Whelan, in which a small fixed current is passed and the prevailing resistance read from a voltmeter graduated in ohms.

In the present study readings were made in a room at 18° C. from 12 points between the root and extremity of each arm or leg of 87 patients undergoing sympathectomy for arterial disease of the particular limb, first before operation, then several weeks after operation, and again much later—up to 3½ years postoperatively. Pre-operatively, the resistance was high at the limb root and fell to a low level at the digits. At the second examination a considerable increase in resistance was noted and was now maximal at the extremity of the limb; there was no change in skin resistance in the intact opposite limb. At the third examination the resistance had fallen, but was usually still notably high. In only one case did the pattern return to the preoperative one. The authors conclude that some regain of sympathetic function in the sweat glands is inevitable, though it may be slow to appear. [No evidence is presented that the regain is in fact mediated by nervous mechanisms.] They incline to the belief that regeneration is a less likely reason for their findings than the slow development of alternative nervous pathways.

C. J. Longland

755. Medical Progress; Neurology. [Review Article] W. K. JORDAN and H. H. MERRITT. *New England Journal of Medicine* [New Engl. J. Med.] 260, 644-652, March 26, 1959 and 702-709, April 2, 1959. Bibliography.

Psychiatry

756. A Follow-up Study of Criminal Psychopaths

T. C. N. GIBBENS, D. A. POND, and D. STAFFORD-CLARK. *Journal of Mental Science* [*J. ment. Sci.*] **105**, 108-115, Jan. [received April], 1959. 5 refs.

With the collaboration of the Prison Commission the authors have followed up over a period of 8 years 72 criminal psychopaths who were either aggressive or predominantly "inadequate" and have compared the results with those in a control group of 59 non-psychopathic prisoners with a criminal record.

It was found that the psychopaths had a greater number of subsequent convictions than the controls, and that the prognosis was worse for aggressive than for inadequate psychopaths. But the prognosis was not invariably bad, since 24% of the psychopaths (most of these being classified as inadequate) had only one re-conviction or none at all. Psychopaths with head injuries had a high proportion of convictions for violent offences. The electroencephalogram (EEG) was abnormal more often among psychopaths than among controls. There was some indication that in inadequate psychopaths and those over 25 years of age an abnormal EEG had a slightly favourable prognostic significance, perhaps because it offered some hope that improvement through maturation might still occur.

A significantly higher proportion of psychopaths than of controls committed aggressive offences, but aggressive psychopaths were much more often convicted of acquisitive than of aggressive crimes, probably, it is suggested, because their social relations are so crippled that they can make a living only by crime. The psychopaths who relapsed did so most often within 6 to 12 months, whereas the controls relapsed at a more even rate throughout the follow-up period. The disconcerting finding that the diagnosis of psychopathy was a less reliable prognostic guide to future criminal acts than the number of previous convictions underlines the fact that "much progress still has to be made in understanding the relation between mental abnormality and criminal behaviour". It is thought possible that psychopaths learn to express their abnormality in other than criminal ways.

F. K. Taylor

757. Prochlorperazine (Stemetil) in Mental Deficiency

T. L. PILKINGTON. *Journal of Mental Science* [*J. ment. Sci.*] **105**, 215-219, Jan. [received April], 1959. 11 refs.

From Glenfrith Hospital, Leicester, the author reports a trial of prochlorperazine ("stemetil") which was carried out on 28 male and 60 female mentally defective patients with severe behaviour disorders. The series included 21 children aged 6 to 14 (average age 10.75 years), of whom all but 3 were low-grade defectives; of the 67 adults, who ranged in age from 15 to 66 years, 42 were low-grade and 25 high-grade mental defectives. The children received the drug in a dosage of 5 mg. three times a day for 2 months and the adults initially

12.5 mg. increasing to 25 mg. thrice daily in 2 weeks and continuing at that dosage for the remainder of the 2 months. Improvement in behaviour followed in 57 patients; affective and simple hyperactive patients showed the best response, schizophrenics the poorest, while epileptics were intermediate. Side-effects occurred in only 2 of the children in the form of slight drowsiness and "pins-and-needles" respectively. In the adults, however, side-effects were more frequent and disturbing, especially among low-grade defectives. In 20 adult patients the dosage had to be reduced or treatment stopped because of rigidity and tremor, excessive drowsiness, severe deterioration of behaviour, dizziness, and headaches. Nevertheless prochlorperazine is considered to be of real value in the treatment of severe behaviour disorders in mentally defective patients, especially those belonging to the affective and hyperactive group.

F. K. Taylor

758. Clinical Trial of Phencyclidine (Sernyl) in Patients with Psychoneurosis

T. BODI, I. SHARE, H. LEVY, and J. H. MOYER. *Antibiotic Medicine and Clinical Therapy* [*Antibiot. Med.*] **6**, 79-84, Feb., 1959.

A trial of phencyclidine ("sernyl") in the treatment of psychoneurotic illness was carried out on 32 patients attending Hahnemann Hospital, Philadelphia, as out-patients. There were 22 women (18 negro) and 10 men (7 negro) ranging in age from 16 to 74 years. The duration of the disorder varied from several months to 6 years. Phencyclidine was given in tablet form, starting with 0.25 mg. thrice daily and increasing the dose at weekly or 2-weekly intervals until symptoms were relieved or side-effects became intolerable. In the latter circumstance the dose was decreased until the maximum tolerable dose was found. After maintenance on a stable dosage for a few weeks placebo treatment was substituted without the patient's knowledge, so that each patient served as his own control.

The criterion of improvement was the subjective alleviation of symptoms. On this basis 15 of the 32 patients showed considerable improvement, 7 slight improvement, and 3 became asymptomatic; the remaining 7 had no improvement. A number of patients felt slight improvement while taking the placebo. The dose that was both best therapeutically and best tolerated varied between 1.5 and 4.5 mg. daily. Side-effects were drowsiness, dizziness, drunken sensations, vomiting, numbness, and in one case a maculopapular rash.

Patients who responded well to phencyclidine were those with anxiety and other psychoneuroses and with psychophysiological reaction of mild or moderate degree, while those with personality disorders and residual schizophrenic reaction responded poorly. The authors consider that the greatest disadvantage of this agent is the narrow range that exists between effective dose and the appearance of side-effects.

E. H. Johnson

Dermatology

759. Topical Therapy with Chlorquinaldol and Hydrocortisone

H. H. FOX. *Antibiotic Medicine and Clinical Therapy* [Antibiot. Med.] 6, 85-90, Feb., 1959. 10 refs.

The author, from the University of Cincinnati, Ohio, reports the treatment of dermatological disorders with an oxyquinoline derivative—chlorquinaldol—in combination with hydrocortisone; the two drugs were also evaluated separately. Chlorquinaldol was used in a 3% concentration, and hydrocortisone in concentrations of 1% and 0.5%. Treatment was by topical application, usually in a water-miscible base, but in a few cases an ointment base was used.

Of 170 patients suffering from eczematous dermatoses or bacterial or fungal infections, treatment with chlorquinaldol alone was effective—the skin condition being much improved or clearing—in 101 (60%). When chlorquinaldol in combination with 1% hydrocortisone was used 166 (82%) of 203 patients were much improved. This combination was found to be more effective than either agent alone. Chlorquinaldol with 0.5% hydrocortisone was effective in 41 (71%) of 58 cases, and in paired comparisons was superior to chlorquinaldol alone and equal to 1% hydrocortisone alone. The only side-effect observed was irritation, which affected 3 of the 289 patients receiving the combination and 11 of the 170 patients treated with chlorquinaldol alone. Sensitivity did not develop in any case treated with the combined drugs, nor did effectiveness decrease with the passage of time. Among the conditions which gave the best response to the treatment were neurodermatitis, atopic eczema, contact eczema, contact dermatitis, infective eczematous dermatitis, and fungal infections.

E. H. Johnson

760. Pustular Acne, Staphylococcal and Its Treatment with Tolbutamide

J. L. COHEN and A. D. COHEN. *Canadian Medical Association Journal* [Canad. med. Ass. J.] 80, 629-632, April 15, 1959. 6 refs.

Shortly after the introduction of tolbutamide for the treatment of diabetes the authors observed rapid recovery from moderately severe acne in 2 female patients undergoing this treatment. The drug was therefore given to 23 further patients with pustular acne vulgaris or other pustular dermatoses which had proved resistant to the usual methods of therapy. Patients with severe acne received 0.5 g. of tolbutamide every 12 hours, while those with less severe acne received 0.5 g. every 24 hours, the duration of treatment ranging from 4 weeks to 4 months.

This treatment failed in one case only, that of a woman who was allergic to sulphonamides. There was improvement in all other cases, this being "fair" in 6 and

"good" or "excellent" in the remainder. Patients were instructed to continue taking carbohydrates while receiving tolbutamide. The fasting blood sugar level, which was determined at intervals in several patients receiving 1 g. daily, was within normal limits.

R. R. Willcox

761. Erythema Nodosum. A Study of Seventy Cases

C. M. R. VESEY and D. S. WILKINSON. *British Journal of Dermatology* [Brit. J. Derm.] 71, 139-155, April, 1959. 3 figs., 40 refs.

After giving a brief outline of the historical background of erythema nodosum, which was first described by Willan in 1798, the authors analyse 70 consecutive cases in order to establish the relative incidence of the three main causes—namely, tuberculosis, streptococcal infection, and sarcoidosis. The cases fell into six main groups as follows: (1) tuberculous—4 cases, the oldest patient being aged 24 years; (2) streptococcal—8 "proved" and 17 "presumed" cases—the main criteria being a preceding tonsillitis and the finding of β -haemolytic streptococci; (3) bilateral hilar-node syndrome without evidence of parenchymatous sarcoidosis—20 cases, average age 32 years; (4) erythema nodosum with pulmonary sarcoidosis—5 cases, average age 42 years; (5) middle-aged women with recurrent bronchitis—7 cases; (6) miscellaneous and unknown—9 cases. Thus of the 70 cases, 45.6% were of proven or presumptive streptococcal origin, 35.7% accompanied sarcoidosis, 13% were of mixed or unknown origin, and only 5.6% were tuberculous. The authors noted depression frequently in patients with disease of the sarcoid type.

E. W. Prosser Thomas

762. Altered L-Methionine S³⁵ Utilization in Psoriasis

M. J. LIPNIK and S. H. LEVY. *Journal of Investigative Dermatology* [J. invest. Derm.] 32, 519-524, April, 1959. 1 fig., 12 refs.

The authors, at Sinai Hospital, Detroit, Michigan, studied the metabolic aspects of the dermis in psoriasis *in vivo*, using as a test substance the biologically active laevorotatory form of methionine labelled with radioactive sulphur (³⁵S) as a tracer substance which could be tracked by counts of radioactivity at the skin surface. The subjects of the study were 9 patients with a severe form of psoriasis, 14 patients with no skin disease serving as controls. The methods and materials used are described and the results obtained discussed and tabulated. The authors conclude that L-methionine-³⁵S is retained by the diseased skin of the patches of psoriasis, but that the affinity for sulphur does not involve the clear skin of the psoriatic patient. The possible cause of the sulphur retention is discussed, but no definite conclusions are reached.

G. B. Mitchell-Heggs

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

763. **Cord-blood Findings in ABO Haemolytic Disease**
G. H. TOVEY, E. M. GILLESPIE, J. GUY, T. VALAES, T. E. OPPÉ, and F. J. W. LEWIS. *Lancet* [Lancet] 1, 860-863, April 25, 1959. 3 figs., 7 refs.

Haemolytic disease of the newborn due to ABO incompatibility, though as frequent as that due to Rh incompatibility, is fortunately usually milder, and the indications for performing an exchange transfusion may be different. For this reason the authors, working at the South-Western Blood Transfusion Centre and Southmead Hospital, Bristol, have studied 575 babies born to mothers of Blood Group O and correlated the cord-blood findings with the clinical progress. The baby was classed "compatible" if its blood was of Group O (393 cases) and "incompatible" if of Group A or B (182 cases). Deep jaundice (a serum bilirubin level higher than 10 mg. per 100 ml.) occurred in 8% of incompatible as compared with 1% of compatible full-term babies, but slight jaundice occurred with about equal frequency in both groups. Of the 92 babies born before the 38th week of gestation but weighing more than 2,500 g., 19% were deeply jaundiced, the incidence apparently being unaffected by the ABO group. The haemoglobin value in cord blood differed little in the two groups, being below 100% (14.8 g. per 100 ml.) in 7 of the incompatible babies and in 13 of the compatible babies. The serum bilirubin level, determined on 212 samples of cord blood, also showed little difference between the two groups; in 7 of the incompatible and 3 of the compatible infants the value was greater than 3 mg. per 100 ml.

On clinical and laboratory evidence 6 babies had haemolytic disease due to ABO incompatibility (all cases of Rh or other types of blood-group incompatibility being excluded from the study), but none required exchange transfusion, though this treatment was required by two compatible premature babies in the series on account of hyperbilirubinaemia. The direct antiglobulin test was positive in only one case, and the haemoglobin value was below 100% in only one. The cord serum bilirubin level was above 3 mg. per 100 ml. in 3 of the 5 in which it was tested; the highest value was 4.7 mg. per 100 ml. and in this infant the maximum level of 9 mg. per 100 ml. was reached in 24 hours. In 5 cases there was clinical jaundice within 24 hours of birth, but none of the infants showed pallor or enlargement of the liver or spleen. The erythrocyte "saline fragility" test of Rosenfield (*Blood*, 1955, 10, 17; *Abstr. Wld Med.*, 1955, 18, 215) and the reticulocyte counts on 113 cord-blood samples of these babies did not help in the diagnosis. The authors conclude that the rate of rise of the level of indirect bilirubin in the blood gives a better indication of

the need for exchange transfusion in haemolytic disease due to ABO incompatibility than the levels of haemoglobin and bilirubin in the cord blood. F. P. Hudson

764. **Oxygen Capacity and Affinity of Blood from Erythroblastotic Newborns. I. Effects of Plasma Environment on Erythrocytes Containing Fetal or Adult Hemoglobin**

A. ABRAHAMOV and C. A. SMITH. *A.M.A. Journal of Diseases of Children* [A.M.A. J. Dis. Child.] 97, 375-379, April, 1959. 1 fig., 25 refs.

The haemoglobins of the adult and the foetus in all species studied have been demonstrated to differ in such respects as resistance to alkaline denaturation, chemical structure, immunological properties, behaviour of monomolecular layers, and electrophoretic mobility. Various workers have reported that human foetal and maternal haemoglobins are unlike haemoglobins from other species in that the oxygen dissociation curve for foetal haemoglobin lies to the right of that for maternal haemoglobin (that is, the affinity for oxygen of the former is less than that of the latter), the opposite being consistently found with other animals. [The dissociation curve for suspensions of human foetal erythrocytes, however, lies to the left of that for suspensions of human adult erythrocytes, the oxygen affinity of the two haemoglobins being affected differently by their respective cell envelopes. (McCarthy, *J. Physiol. (Lond.)*, 1943, 102, 55.)—EDITOR.] However, Allen *et al.* (*J. biol. Chem.*, 1953, 203, 81) have reported that after dialysis human foetal and maternal haemoglobin give identical dissociation curves and have suggested that the reported differences "may result from difference in the environment of the hemoglobin molecule". This environment is primarily that enclosed by the cell membrane of the erythrocyte, but the oxygen affinity of the haemoglobin may be affected by diffusible elements of the plasma. To test this possibility the effect of neonatal plasma upon adult erythrocytes and vice versa was investigated at the Boston Lying-in and Children's Hospitals (Harvard Medical School). Oxygen dissociation curves were determined with blood from 10 erythroblastotic newborn infants at birth, and in all cases were in the expected position to the left of the curve from adult blood. Five to 7 days after exchange transfusion, when the infants' haemoglobin was of the adult type and the plasma had had time after the transfusion to resume its usual neonatal form, the oxygen dissociation curve had shifted to the right into the normal adult range. Compatible blood from 3 normal adults and 3 normal newborn babies was then taken and the erythrocytes of each adult suspended in the plasma of one of the babies and vice versa, the haematocrit being adjusted to normal levels. Oxygen dissociation curves for these mixtures showed that both newborn and adult erythrocytes

retained their special characteristics despite the change in plasma environment. It is pointed out that no blood specimens were obtained from infants before birth, but as there is no evidence that the plasma changes significantly even within a few hours after birth the evidence obtained from neonatal specimens "presumably applies to the foetal situation".

It appears therefore that erythrocytes containing foetal haemoglobin do not require a foetal plasma environment for the development of their typical oxygen dissociation curve and that such an environment does not affect the oxygen dissociation of adult haemoglobin. That the substitution of adult erythrocytes by exchange transfusion shifts the newborn infant's characteristically "foetal" oxygen affinity to the right is of interest in view of the known safety of this procedure in the treatment of erythroblastosis or hyperbilirubinaemia. Whatever its advantages, the "foetal" oxygen dissociation curve is evidently not essential for neonatal life.

An additional finding in this study was that the haemoglobin of newborn infants with Rh incompatibility contained in erythrocytes coated with "blocking" antibodies was reduced in oxygen-carrying capacity by 15 to 31%. This deficiency may be worth taking into consideration in deciding whether or not to undertake exchange transfusion with normal cells of higher oxygen capacity.

J. Browne Kutschbach

765. Reduction of Oxygen-carrying Capacity of Rh-positive Erythrocytes Coated with Anti-D Antibodies

A. ABRAHAMOV and L. K. DIAMOND. *A.M.A. Journal of Diseases of Children* [A.M.A. J. Dis. Child.] 97, 380-383, April, 1959. 6 refs.

The observation previously reported [see Abstract 764] that the oxygen-carrying capacity of the blood of newborn infants with erythroblastosis due to Rh incompatibility was significantly less than that to be expected from its haemoglobin concentration suggested a hitherto unsuspected effect of "blocking" antibodies upon the erythrocytes. Antibodies of this type are incapable of agglutinating erythrocytes suspended in saline, but combine with cells containing the proper receptor, thus rendering them insusceptible to agglutination by ordinary agglutinins.

In the present study the effect of anti-D antibodies on the oxygen-carrying capacity of Rh-positive erythrocytes from 30 specimens of Group-O blood was studied. The simple addition of anti-D serum to the erythrocytes did not by itself reduce their oxygen-carrying capacity, although the direct Coombs test showed them to be coated immediately with the antibodies. Two further factors were necessary—a temperature of 37° C. and a time lapse of 12 to 24 hours. It was noted that Rh-positive erythrocytes treated with anti-D serum retained their shape and underwent no loss of oxygen-carrying capacity when treated for less than 12 hours or when incubated at 4° C., but after treatment for 12 to 24 hours at 37° C. they became crenated and their affinity for oxygen was markedly reduced. There was no haemolysis and no agglutination. The authors suggest that the antibodies damage the cell membrane in some way,

lessening its permeability to gases and thus interfering with oxygen uptake. There was nothing to suggest that the anti-D serum caused any change in metabolic or enzymatic activity within the erythrocyte, but they intend to investigate this possibility more thoroughly.

J. Browne Kutschbach

766. Hyperbilirubinaemia and Kernicterus in Premature and Full-term Bantu Newborn Infants

M. H. SHNIE and S. E. LEVIN. *British Medical Journal* [Brit. med. J.] 1, 1004-1007, April 18, 1959. 1 fig., 27 refs.

In this paper from the University of the Witwatersrand attention is drawn to the high incidence of hyperbilirubinaemia and kernicterus in Bantu infants. Of 5,000 consecutive newborn Bantu infants, 211 were seen to have jaundice within 36 hours of birth or severe jaundice between the second and seventh days of life. (Rhesus incompatibility, which is rare in the Bantu, caused jaundice in 4 infants, and these were excluded from this series.) Of the 211 infants, 148 weighed 5½ lb. (2.5 kg.) or less at birth. The time at onset of jaundice varied with the birth weight, only 10% of infants weighing 2 to 3 lb. (0.9 to 1.4 kg.) being jaundiced within 36 hours as compared with 60% of the full-term infants. Kernicterus, which developed in 14 patients, only 3 of whom survived, was diagnosed on the second day of life in one, on the fourth day in 5, on the fifth day in 4, and on the sixth day in 3; the time at onset in one case was uncertain. The serum bilirubin level in all these infants was above 15 mg. per 100 ml., and in the 2 full-term infants it was 20.5 and 35 mg. per 100 ml. respectively. Diarrhoea and dehydration developed in 6 of the premature babies and was associated with a rapid rise in the serum bilirubin level. The authors state that the serum bilirubin level can be used as an indication for exchange transfusion only if related to the birth weight; they suggest the following: 15 mg. per 100 ml. in infants weighing 3 to 3½ lb. (1.4 to 1.6 kg.) at birth; 16 mg. per 100 ml. with birth weight up to 4½ lb. (2.4 kg.); 18 mg. per 100 ml. with birth weight up to 5½ lb. (2.5 kg.); and 20 mg. per 100 ml. with birth weight over 5½ lb. It is emphasized that in the Bantu races kernicterus of prematurity presents a greater problem than kernicterus due to haemolytic disease.

E. P. Hudson

767. Sulphobromophthalein Excretion in Premature Infants

T. E. OPPÉ and I. E. GIBBS. *Archives of Disease in Childhood* [Arch. Dis. Childh.] 34, 125-130, April, 1959. 3 figs., 20 refs.

"Physiological" jaundice of the newborn is probably due to absence of the enzyme systems responsible for the synthesis of glucuronide in the liver. As sulphobromophthalein (BSP) is believed to be excreted by the liver as a glucuronide the excretion of BSP was studied in 34 premature infants, 14 being less than a day old, 10 aged 5 days, and 10 aged 14 days. Selection was based mainly on postnatal age, but ill children and infants whose low birth weight might have been due to causes other than prematurity were excluded. Jaundice, unless there was

evidence of haemolytic disease, was not a contra-indication. Intravenous injection of BSP, 5 mg. per kg. body weight, was followed by an estimation of capillary blood content after 5, 10, 30, 45, and 60 minutes. By plotting log. BSP content against time a two-phase excretion, shown as two straight lines, was demonstrated. There were highly significant differences in the second phase between the 3 age groups, suggesting that by 21 days excretion of BSP should be at about adult level. Degree of prematurity had no effect on this improvement of excretion with postnatal age. Presence or absence of jaundice did not affect the change towards adult excretion. On the other hand 2 infants with obstructive jaundice gave an excretion curve similar to that of the one-day-old infants. Even slight respiratory embarrassment at birth had a marked effect on BSP excretion in the one-day-old infants.

The evidence suggests that the development of the excretory mechanism for BSP is part of the physiological process of adaptation to extra-uterine life rather than just a function of maturity.

E. H. Johnson

CLINICAL PAEDIATRICS

768. Investigation into the Aetiology and Treatment of Pica

P. LANZKOWSKY. *Archives of Disease in Childhood* [Arch. Dis. Childh.] 34, 140-148, April, 1959. 41 refs.

Pica is a perversion of appetite in which the subject persistently and purposely ingests unsuitable substances, commonly earth, stones, or sand. After a summary of the literature 12 cases of pica seen at the Red Cross Hospital, Cape Town, South Africa, during a 5-month period are described. Of the 12 patients, 10 were Cape coloured and 2 white, 7 being girls and 5 boys; their ages ranged from 1 year 8 months to 6½ years. Pica had persisted for 6 months to 3½ years. In 7 cases advice was sought for the condition itself, and in the others for diarrhoea (2), abdominal pain, worms, and an abdominal mass with anaemia (one each). Nearly all the children were well nourished. Two had temper tantrums, but the rest were well behaved. All except 2 had worms. Intelligence was normal or above normal. Haemoglobin levels varied between 3.0 g. and 10.9 g. per 100 ml. The usual blood picture of secondary anaemia was present in the more severe cases.

Treatment consisted in intramuscular injection of a large dose of iron-dextran compound ("imferon"); one child was given ferrous gluconate by mouth. In only one case was there no improvement in haemoglobin level, the mean in the others rising from 7.89 g. to 11.34 g. per 100 ml. and a complete cure of the pica being obtained after treatment lasting 1 to 2 weeks. No other treatment than the administration of iron was given. The children had ample opportunity to continue the perversion, but gave it up. No treatment was given in any case for the helminthiasis. The case in which cure was not recorded was the one with an abdominal mass, which proved to be a lymphosarcoma and was fatal.

E. H. Johnson

769. A Patch Test for Chloride in Sweat as a Simple Screening Method for Detecting Cystic Fibrosis of the Pancreas: Preliminary Report

L. GLUCK. *Pediatrics* [Pediatrics] 23, 731-737, April, 1959. 1 fig., 15 refs.

A simple patch test is described for the detection of cystic fibrosis of the pancreas based on estimation of the concentration of chloride in the sweat rather than the amount of chloride on the skin at any given time. Gelatin is employed because of its properties as a reversible hydrophilic colloid, and the objective of the patch test is to bring out a colour change when the concentration of chloride in the sweat is 50 mEq. per litre or more. A clear film of silver nitrate and potassium chromate is coated on to one surface of the gelatin. A patch of this gelatin is then applied to the palm of the patient's hand (which has been thoroughly washed and dried to remove sweat) and covered with clear plastic tape in order to observe colour changes and to judge whether there is adequate sweating. The response is considered to be positive when the numerous sweat droplets appear as yellow images along the lines of the palm.

The results obtained with this patch test in 118 children were, with the exception of one false positive response, in accord with those of quantitative chemical analysis of the sweat. Interpretation of the patch test was seldom troublesome, but certain errors and limitations are briefly discussed. Of the several patients with chloride concentrations in the sweat between 40 and 50 mEq. per litre, none gave a positive reaction to the patch test, and none of the patients with a chloride concentration greater than 50 mEq. per litre gave a negative response. The physiology of sweating, particularly in relation to the diagnosis of disease in children, is discussed.

J. M. Smellie

770. Renal Tubular Damage in Infantile Gastro-enteritis

J. BLACK. *Archives of Disease in Childhood* [Arch. Dis. Childh.] 34, 158-165, April, 1959. 3 figs., 28 refs.

There are few reports in the literature of renal tubular damage in children, although the conditions producing circulatory collapse and shock with consequent renal ischaemia are far from rare in infancy and childhood. Acute gastro-enteritis is the most frequent cause of severe dehydration and shock in infancy, but the literature on renal tubular damage in this condition is also scanty. In this paper from the Hospital for Sick Children, Great Ormond Street, London, the author describes 2 cases of acute infantile gastro-enteritis in which renal tubular damage was noted. Both infants were extremely ill, dehydrated, and shocked, and although they recovered, there was very definite evidence of renal tubular damage. A retrospective survey of 653 cases of acute gastro-enteritis seen at the same hospital showed that in 21 the concentration of protein in the urine was over 40 mg. per 100 ml.

It is suggested that in infants and children with gastro-enteritis evidence of renal tubular damage should be looked for more closely, special attention being paid to the phase of diuresis if dehydration and electrolyte depletion are to be avoided.

John Fry

771. Lymphopneumatosis Cystoides Intestinalis with Eosinophilia in the Infant

J. GAGNON and M. RHEAULT. *Pediatrics* [*Pediatrics*] 23, 710-717, April, 1959. 5 figs., 14 refs.

The manifestations of lymphopneumatosis cystoides intestinalis are described and the history and necropsy findings in 5 infants, aged 15 days to 5 months, are reported in this paper from Sainte-Justine Hospital, Montreal. In the organs responding to "stress" there were severe non-specific lesions. Many of the lymphocytes in the thymus and the spleen showed pyknosis, and in the periphery of the splenic follicles numerous eosinophils were observed. The perirenal and perivisceral adipose tissue showed acidophilic fat cells full of cytoplasm. The bone marrow contained an abundance of eosinophilic myelocytes and eosinophilic polymorphonuclear leucocytes. Gas cysts present in the submucosa of the intestine caused the mucosa and muscularis externa to bulge, but these cysts did not contain bacteria. In 2 cases gas cysts were also present in the mesenteric lymph nodes, and eosinophils were seen in the sinuses and at the periphery of the nodes.

The authors state that the pathogenesis of the disease is obscure, many theories having been advocated but none substantiated. Factors which appear to be associated are gastro-intestinal disturbances, generally accompanied by infection, and acidification of the gastro-intestinal contents. Eosinophilia does not seem to be produced by the gases in the cysts. J. M. Smellie

772. Metabolic Consequences of Pancreatic Insufficiency in Cystic Fibrosis of the Pancreas: a Statistical Analysis

C. U. LOWE and V. PESSIN. *Pediatrics* [*Pediatrics*] 23, 738-752, April, 1959. 1 fig., bibliography.

773. Systolic Murmurs in Children. A Survey of 240 Cases.

W. MAINZER, R. PINCOVICI, and G. HEYMANN. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] 34, 131-136, April, 1959. 1 fig., 15 refs.

Of 2,035 children from rural settlements in the Haifa area, 240 (11.8%) had systolic murmurs. The incidence rose suddenly at the age of 5 years and remained relatively high between 5 and 10 years. At all ages slightly more male children had murmurs than female. It was noted that 40% of all cases occurred in siblings, and it was estimated that if the parents were included familial incidence would be still higher, as parents of several of these siblings were known to have systolic murmurs. The highest incidence of murmurs was found among children of Mediterranean origin. It was somewhat lower among children of Western origin and definitely lower among those from India.

Of the 240 cases, the murmurs in 154 (64.2%) were classed as "innocent"—that is, associated with no indication of heart disease in the history or on physical, laboratory, fluoroscopic, or electrocardiographic examination. A further 47 cases (19.5%) were classed as of "possible heart disease"—that is, with suggestive signs, but without any conclusive evidence of structural

change. In 31 cases (13%) the murmurs were attributed to "probable heart disease", the evidence indicating structural change in the heart, though no definite diagnosis could be made. In only 8 cases (3.3%) could heart disease be definitely diagnosed. No physical criterion, such as intensity, location, or constancy of the murmur, was diagnostic of a pathological or innocent origin. It is suggested that a thorough examination, including laboratory tests, electrocardiography, and fluoroscopy, is necessary in each case to arrive at a proper distinction. E. H. Johnson

774. Chronic Bronchitis as a Sequel of Whooping Cough. (Les bronchites chroniques post-coquelucheuses)

J. M. LEMOINE and J. DENIS. *Presse médicale* [*Presse méd.*] 67, 768-771, April 18, 1959. 1 fig., 30 refs.

At the Hôpital Cochin, Paris, the authors have studied the aetiological relationship between pertussis and chronic bronchitis in a series of 36 patients in whom a refractory cough had appeared shortly after an attack of whooping-cough and who had not previously been subject to respiratory disorders. A clinical, radiological, and bronchoscopic examination was made within a few months of the attack in 11 cases, within one to 5 years in 6, and within 6 to 30 years in 19. There were only 9 males among the 36 patients, most of whom were children aged 3 to 14, though 10 were over 25. The presenting symptom was cough in 34 cases and a recent haemoptysis in 2. In 9 the cough occurred most frequently at night and in characteristic spasms reminiscent of whooping-cough, while in the remainder there were frequent and exhausting bouts of coughing at irregular periods throughout the day, brought on by a variety of alleged causes. In 17 cases the cough was dry, hacking, and non-productive. In the remaining 19 it was accompanied by sputum (up to 100 ml. a day), usually viscid in consistency, translucent or opaque in appearance, white, grey, or green in colour, and only rarely purulent. The sputum varied both in quantity and in quality from patient to patient and in the same patient from time to time. The over-all health of the group was excellent. Neither loss of weight nor pyrexia was often observed.

Radiography of the chest showed normal appearances in 15 cases, increased and irregular hilar shadows in 4, nodular opacities collected chiefly around the hila in 8, and homogeneous shadows clearly limited to one or two lobes, with signs of retraction, in 9. Bronchoscopy revealed not only that bronchial inflammation was present in all 36 patients, but that it was more widespread and diffuse than was suggested by the x-ray appearances. On the other hand bronchial suppuration was less frequently encountered than the radiographs had led the authors to expect. The larger bronchi were affected more often than the smaller, and those of the right side more often than those of the left. Tracheal involvement was seen in 7 cases only and never as an isolated phenomenon. The mucosa never had the vivid red colour met with, for instance, in heavy smokers; it was glossy in appearance and thickened, so that the bron-

chial lumen was much reduced. Sticky, adherent bronchial secretion was always present.

Bronchoscopy was always followed by abatement or disappearance of the cough within 2 to 30 days. When it was combined with aspiration of secretions or local application of adrenaline to the inflamed mucous membrane radiological and clinical improvement was even more marked. A single bronchoscopy was sufficient in 26 cases; owing to the return of the cough after a quiescent spell it was repeated once in 6 cases, twice in 2, and more often in 2 others, being followed on each occasion by improvement as rapid as after the initial examination.

The authors conclude that chronic bronchitis occurs as a sequel of whooping-cough in a few cases. But although the ability of *Haemophilus pertussis* to cause acute bronchitis was demonstrated by bronchoscopy in 2 cases in adults at the height of the attack, they do not regard this sequel as specifically due to infection with *H. pertussis*—or to bacterial infection at all unless this is superadded. In their opinion the condition is due to a condition of allergy to a number of non-specific stimuli which is set up in the mucosa as a result of the initial infection by *H. pertussis*.

E. S. Wyder

775. Lung Volumes of Normal and Asthmatic Children
J. F. ANDREWS and D. H. SIMMONS. *Pediatrics* [Pediatrics] 23, 507-519, March, 1959. 10 figs., 13 refs.

Various measurements of pulmonary function between attacks were carried out on 21 asthmatic children aged 6 to 15 years who were attending allergy clinics in Los Angeles and Santa Monica, similar observations being made on a control group of 27 normal children aged 6½ to 13 years. The object of the investigation was to determine whether the hyperinflation of the lungs which can be demonstrated during periods of clinical freedom from attacks in adults and older children with asthma is also present in younger children. It was further hoped to draw conclusions from the results as to the nature of the persistent bronchial obstruction which has been suggested as a possible cause of hyperinflation of the asthmatic's chest. For this purpose the tests were repeated on some of the children after the administration of an isoprenaline aerosol.

The closed-circuit helium-dilution method was used to measure total lung capacity, mixing efficiency in the lungs, functional residual capacity, residual volume, and vital capacity. In the asthmatic group there was a significant increase as compared with the control group in all the values except the mixing efficiency, which was considerably impaired in most cases, and the vital capacity, which was decreased in 5 cases. The values showed little change after administration of isoprenaline, but it was thought that the dosage might have been inadequate. No correlation could be found between the length of history of attacks and the degree of impairment of function, but the authors suggest that it is possible that the hyperinflation occurring in asthmatic children is due to bronchospasm and is reversible, whereas in adult patients it is due partly to structural change.

K. M. Hume

776. Types of Exstrophy of Urinary Bladder and Concomitant Malformations: a Report Based on 82 Cases
A. C. USON, J. K. LATTIMER, and M. M. MELICOW. *Pediatrics* [Pediatrics] 23, 927-934, May, 1959. 13 refs.

The incidence and types of exstrophy of the urinary bladder and the malformations associated with this condition were studied in the case records of 72 children seen at the Babies Hospital and the Squier Urological Clinic, Columbia-Presbyterian Medical Center, New York. Complete exstrophy was present in 66, the characteristic findings being protrusion of the complete posterior wall of the bladder, ventral hernia, wide separation of the symphysis pubis and recti, complete epispadias, cleft clitoris, and absent or unroofed urethra. In 4 patients there was exstrophy of the cloaca characterized by intestinal fistula and prolapse of the intestine; this type of exstrophy is invariably fatal. The rarest type is incomplete exstrophy (2 patients only), in which the space between the umbilicus and the symphysis is reduced and there is an omphalocele with protrusion of the uncovered anterior surface of the bladder; one of the patients (male) had a flattened penis and the other (female) a recto-vaginal fistula.

Associated abnormalities, which were common, included inguinal hernia, undescended testicle, vaginal malformation, duplication of the upper urinary tract, hydronephrosis, rectal prolapse, spina bifida, congenital heart disease, cleft palate, and mongolism. The treatment of the condition is discussed. Charles Nicholas

777. A Fatal Granulomatous Disease of Childhood. The Clinical, Pathological, and Laboratory Features of a New Syndrome

R. A. BRIDGES, H. BERENDES, and R. A. GOOD. *A.M.A. Journal of Diseases of Children* [A.M.A. J. Dis. Child.] 97, 387-408, April, 1959. 13 figs., 22 refs.

A fatal clinical syndrome not previously described in the literature was seen in 4 children (all males) at the University of Minnesota Hospitals, Minneapolis. The chief clinical features of the disease, which ran a protracted course (5 years in one case), were widespread chronic suppurative lymphadenitis, an eczematoid dermatitis affecting especially the face, eyelids, and around the nose, a chronic relapsing conjunctivitis, and extreme debilitation. In the later stages severe chronic pulmonary infection developed and the liver and spleen were enlarged. There was a marked polymorphonuclear leucocytosis with severe anaemia, and the erythrocyte sedimentation rate was persistently raised. A constant feature of the electrophoretic pattern of the serum proteins was a distinct increase in the α_2 - and γ -globulin fractions. A marrow plasmacytosis was present in all cases. Repeated attempts to isolate an aetiological agent were unsuccessful, and the response to intradermal injection of special skin-test antigens was inconclusive. Immunological capacity and leucocyte function in these children were normal. A variety of treatments were tried, but without avail. The authors consider that the syndrome described bears a resemblance both to infections and to the reticulo-endothelioses.

Winston Turner

Public Health and Industrial Medicine

PUBLIC HEALTH

778. An Investigation of the Validity of Death Certification of Cancer of the Lung in Leeds

G. M. BONSER and G. M. THOMAS. *British Journal of Cancer* [Brit. J. Cancer] 13, 1-12, March, 1959. 6 refs.

The first part of this survey, reported from the University of Leeds, consisted in a review of the 1,036 deaths certified in Leeds in 1950-4 as due to cancer of the trachea, pleura, lungs, or bronchi, and in the successful tracing of the clinical records of all but 37. Of the remaining 999 cases, 35 (3.5%) were incorrectly certified—in only 9 of these was there no cancer present—and in 964 cases (96.5%) the cause given in the death certificate tallied with the clinical diagnosis; in 477 cases (50%) diagnosis was based on histological, cytological, or necropsy findings, in 429 (45%) on ancillary methods without histology, and in 47 (5%) on physical examination and history only; in the other 11 cases the case notes were lost, but the diagnosis was confirmed.

The second part of the survey consisted in a comparison of the clinical notes and death certificates in 879 cases of lung cancer admitted to two Leeds hospitals in 1950-4. Of these patients, 813 (92.5%) were certified as having cancer of the lung at death; in the 66 instances (7.5%) where the clinical diagnosis failed to appear on the death certificate the words "carcinoma of the lung" were either not entered or appeared in a form or position causing difficulty in coding.

Analysis of the 338 cases diagnosed or certified as carcinoma of the lung which were examined post mortem showed that 184 cases (54%) were diagnosed correctly clinically, that 127 were revealed at necropsy, and that in only 27 (8%) was a false positive clinical diagnosis made. No sex difference in accuracy of certification was established.

F. T. H. Wood

779. An Epidemiological Study of Congenital Malformations in New York State

J. T. GENTRY, E. PARKHURST, and G. V. BULIN. *American Journal of Public Health* [Amer. J. publ. Hlth] 49, 497-513, April, 1959. 5 figs., 16 refs.

An investigation is reported of the incidence of congenital malformations in children born in New York State (excluding New York City) between 1948 and 1955 and the relationship, if any, to the distribution of natural materials of relatively high radioactivity.

A total of 16,369 malformations were reported in birth and death certificates during the period, a rate of 13.2 per 1,000 live births. Exceptionally high rates, up to 20.0 per 1,000, were noted in 186 of the 942 townships, especially in certain contiguous areas on high ground. From an examination of geographical and geological data it was possible to define areas with deposits of materials of high radioactivity. The inci-

dence of congenital malformations was greater (15.8 per 1,000 live births) in areas with high levels of natural radioactivity than in rural areas with low levels (12.9 per 1,000). Further, the incidence of malformations in areas of "probable" radioactive materials was higher in communities using water from wells and springs than in those in the same areas using surface water. Measurement of external radiation in areas close to exposed radioactive mineral showed that this was 30 times higher than normal.

Since no other factors were found to be responsible for the varying incidence of congenital malformations, the authors conclude that it is significantly related to local levels of radioactivity.

[This important paper requires confirmation from other parts of the world.]

John Fry

780. Discovery of Typhoid Carrier by Sewage Sampling

L. A. SHEARER, A. S. BROWNE, R. B. GORDON, and A. C. HOLLISTER. *Journal of the American Medical Association* [J. Amer. med. Ass.] 169, 1051-1055, March 7, 1959. 1 fig., 9 refs.

An account is given from the California State Department of Public Health of the use of sewer swabs to locate a typhoid carrier in a city with a population of 2,200. The investigation took place in 1956 following the occurrence of the fourth case of typhoid fever in a period of 5 years. Gauze swabs were lowered into the sewage effluent through "key" manholes throughout the city and allowed to remain in position for 48 hours. At the end of that period they were recovered and cultured for *Salmonella typhosa*. A number of positive cultures were obtained of an organism which on phage typing proved to be of Group D and in addition was lysed by a phage identified as Utrecht 9. This type had caused a number of cases of typhoid fever in the Netherlands, but had not previously been isolated in the U.S.A.

The organism from a case of typhoid fever diagnosed in the city in 1955, which had previously been "untypable", was now re-examined and found to be lysed by Utrecht 9. Examination of sewage from the house in which this ex-patient lived was negative. The results obtained from sewer swabs elsewhere in the city appeared to implicate the local hospital and a block of houses in a certain street. Inquiries along more conventional epidemiological lines revealed that a resident of this street had recently been treated in the hospital for hypertension and cardiac failure. This patient had in early life been a sailor and at one time had stayed in the same house as a man from the Netherlands who was suffering from typhoid fever. Although the patient denied previous illness, he was found to be excreting *S. typhosa* of the same phage type as that isolated from the sewers.

The authors were also able to demonstrate that the grease which accumulates on the inside of sewers may act as a trap for typhoid organisms. "Wipes" of this

grease yielded a number of positive cultures, and further investigations are being carried out to see whether this method is effective enough to eliminate the necessity of laying down sewer swabs.

A. E. Wright

781. **Poliomyelitis Vaccine Preparation and Administration. Analysis of Basic Premises and Current Practices** J. E. SALK. *Journal of the American Medical Association [J. Amer. med. Ass.]* 169, 1829-1838, April 18, 1959. 15 refs.

Experience through 5 seasons has shown that paralytic poliomyelitis does still occasionally occur in persons vaccinated with 3 doses of the formalin-inactivated poliomyelitis virus vaccine. The possible theoretical explanations for this are: (1) the particular batch of vaccine administered may have been of less than optimal potency; (2) the particular individuals may have been unusually unresponsive; (3) the initially induced protective effect may have waned with time; (4) the virus may have reached the central nervous system by another route than the blood stream; and (5) the paralyzing disease may have been caused by a viral agent different from those in the vaccine. Observations have shown that when vaccines of relatively high potency are used for the primary and booster doses adequate responses are obtained for Type 2 in almost all and for Types 1 and 3 in a high proportion of individuals, and little or no decline in the antibody titre occurs between one and 2 years after the booster dose. When vaccines of low antigenic concentration or doses of less than 0.5 ml. of potent vaccine are used, although the tendency for the antibody titre to remain relatively constant between one and 2 years after the booster dose is the same, the level is very much lower and frequently inadequate.

A survey in 1958 covering 2,709 children in the first 3 grades of school who were said to have had 3 doses of vaccine revealed that 9.1% had no detectable antibody to Type 1, 0.5% had none to Type 2, and 18.7% had none to Type 3. A 4th dose of selected vaccine induced a substantial response in 462 of these children who had no antibody to one or more types. The weight of evidence suggests that low levels of antibody for Types 1 and 3 are not due to waning immunity, but to failure to induce a change initially as a result of the use of vaccines of less than optimal potency, and that this is probably the chief cause of the occurrence of paralytic poliomyelitis in triply vaccinated persons.

In 1958 viral agents were isolated from the stools of 75 out of 103 patients with paralyzing illnesses who had been triply vaccinated; 55 of these were polioviruses—Type 1, 39; Type 3, 15; and Types 1 and 3, 1—while the rest were Coxsackie or E.C.H.O.-9 viruses. As the ratio of Type 1 to Types 2 or 3 in paralytic poliomyelitis used to be 8 to 10:1, it would appear that vaccination has been effective for Type 2 and that the effect on Type 1 has been greater than on Type 3.

It is concluded that the solution of the problem of vaccination against poliomyelitis is not the use of multiple doses of weak vaccine, but rather to ensure that all vaccines may be expected to induce, after 2 doses, effects of an order of magnitude that will bring about a con-

dition for Types 1 and 3 that vaccination may already have induced for Type-2 poliomyelitis. A. Ackroyd

782. **Response of Infants to a Third Dose of Poliomyelitis Vaccine Given 10 to 12 Months after Primary Immunization**

F. T. PERKINS, R. YETTS, and W. GAISFORD. *British Medical Journal [Brit. med. J.]* 1, 680-682, March 14, 1959. 3 figs., 5 refs.

The authors have previously reported (*Brit. med. J.*, 1958, 2, 68; *Abstr. Wld Med.*, 1959, 25, 6), that the response of 88 infants to 2 doses of poliomyelitis vaccine starting at the age of 1 week (Group A), 6 weeks (Group B), or 10 weeks (Group C) was in most cases unsatisfactory. They now report the response to a third dose of vaccine given to 80 of them at 10 to 12 months. Since at this time 17 infants had a higher antibody titre against at least one type of virus than they had had immediately following the second dose of vaccine and their response to the booster dose was very high, they were assumed to have had an intercurrent non-paralytic poliomyelitis infection and were excluded from the study.

All those infants who had responded to primary immunization responded to the booster dose; all had had low levels of maternally transmitted antibody. Of the 22 infants in Group A, none of whom had been primary responders, only 5 showed a small increase in antibody titre against Type-1 virus. In Groups B and C the responses to Type-1 virus were greater, 20 of the 32 non-responders showing a rise in titre, but the level of response in many of the infants was not as high as should have occurred if they had been sensitized by the primary immunization. The response to Types 2 and 3 of these 32 infants was better, only 7 in all failing to respond, but again the infants in Groups B and C reacted better than those in Group A. Those infants with high levels of maternally transmitted antibody at birth gave no primary response and did not react to the booster dose. A number with intermediate titre levels (32 to 1,024) of maternally transmitted antibody, even though they gave no apparent primary response, reacted to the booster dose. However, there were also a number with low levels of transmitted antibody who were poor primary responders and also gave a poor response to the booster dose. It is concluded that the earliest age when satisfactory mass immunization can be achieved is probably 6 to 9 months.

A. Ackroyd

783. **A Comparison of the Responses of 100 Infants to Primary Poliomyelitis Immunization with Two and with Three Doses of Vaccine**

F. T. PERKINS, R. YETTS, and W. GAISFORD. *British Medical Journal [Brit. med. J.]* 1, 1083-1086, April 25, 1959. 3 figs., 2 refs.

In continuation of the investigations previously reported [see Abstract 782] the authors carried out further studies (1) on 45 babies one week old to ascertain to what extent the inhibiting effect of maternal antibodies on the response to vaccination could be overcome by

increasing the number and size of the doses, and (2) on 55 infants 16 weeks old to determine whether at this age the baby's own immunological activity was sufficient to overcome that inhibiting effect and also whether a better basal immunity could be obtained with 3 doses than with 2. Two vaccines, distributed equally, were used in each group. Both contained the MEF-1 (Type-2) and Saukett (Type-3) strains, but the Type-1 strain in one was Brunenders and in the other Mahoney. The two vaccines showed similar antigenic activity in monkeys.

In Group 1 36 babies received 3 doses and 9 babies 2 doses of 2 ml. each at 4-week intervals; serum was taken initially from the cord blood, then 4 weeks after the 2nd dose (that is, at the time of the 3rd dose if given) and 14 to 21 days later. In Group 2 all the babies were given 3 doses of 1 ml. each at 4-week intervals, serum being taken from the cord blood and before the first dose and again after the 2nd dose (in 49 cases), after the 3rd dose (in 49 cases), and 14 to 21 days later (in all cases). Only 5 of the 100 infants had no antibodies at all in the cord blood and no less than 59 had antibodies to all 3 types, though the titres varied remarkably, ranging between 8 and more than 16,000, for each type. At age 16 weeks there was 95% loss of maternal antibody. The response of Group 1 to vaccination was generally poor, but was rather better after 3 doses than after 2; a number of babies showed no apparent response, especially to Type 1. The babies in Group 2 responded better to 3 doses than to 2, whether they possessed maternal antibodies or not.

The authors conclude that since even at 16 weeks maternal antibodies, especially to Type 1, may still be present, it is advisable to delay vaccination against poliomyelitis until these antibodies have fallen to a level at which they are unlikely to interfere with immunization, that is, until about 6 to 9 months of age, when 3 doses of vaccine should be given.

[There appears to have been no noticeable difference between the response to the Brunenders Type-1 strain and to the more virulent Mahoney strain.]

W. K. Dunscombe

784. Antibody Response of Adolescents and Adults to a Booster Dose of Poliomyelitis Vaccine

BIOLOGICAL STANDARDS CONTROL LABORATORY, MEDICAL RESEARCH COUNCIL. *British Medical Journal* [Brit. med. J.] 1, 609-613, March 7, 1959. 7 figs., 10 refs.

As previously reported (*Brit. med. J.* 1957, 2, 1207; *Abstr. Wld Med.*, 1958, 23, 301), children under 10 who have no detectable antibody against Type-1 poliomyelitis virus after primary immunization tend to give a poor Type-1 response to a third (booster) dose. It is now reported that a third dose of vaccine given 6 to 12 months after the primary immunization to 88 adolescents and 25 adults produced a poor antibody response to the Type-1 virus in those who had no detectable antibody to this component, although responses to Types 2 and 3 were as satisfactory as in the young children. One-third of the subjects had lost their antibody to Type 1, whereas only 4 individuals had done so to the other two types. In those who still had antibody, delay in giving the booster until 9 to 12 months after the

primary immunization resulted in better antibody responses to Types 1 and 2, but made no appreciable difference to the response to Type 3.

A fourth dose of vaccine given to some of the poor responders 9 months later appeared to produce a booster response to the Type-1 component. Increasing the amount of the Type-1 component in the vaccine two-fold in a group of 22 "triple negative" adults increased their mean geometric Type-1 titre appreciably compared with a similar group of 24 adults given a trivalent vaccine of slightly lower potency than the routine vaccine. A booster dose with a routine vaccine 3 to 4 months later produced an excellent antibody response to Type 1 in the former group, whereas in the latter group the response was similar to that which occurred in the adolescents. It is suggested that the increase in the response to Type-1 virus which would appear necessary in adolescent and adult age groups could be obtained by doubling or preferably trebling the amount of Type-1 antigen in poliomyelitis vaccine.

A. Ackroyd

785. Prevention of Brucellosis. (Профилактика бруцеллеза)

I. K. KARAKULOV, N. F. ZENKOVA, and A. M. BEKETAEVA. *Клиническая Медицина* [Klin. Med. (Mosk.)] 37, 40-44, March, 1959. 15 refs.

The universal distribution of brucellosis, the multiple portals of entry, and the absence of sufficiently effective, specific, and readily available methods of treatment all increase the importance of prophylactic measures against this disease. The authors state that at various periods brucellosis was responsible for up to 13% of all working time lost due to ill health in the Stalingrad district, 16.8% in the district of Rostov, 19% in Uzbekistan, 23% in Kirgizstan, and 37% in Kazakhstan. In cattle-raising areas even the inhabitants of the towns were seriously affected. This fact was insufficiently recognized when prophylactic measures were planned, but specific prophylaxis with a live vaccine of a highly immunogenic strain of *Brucella abortus*, non-pathogenic for man, has been an important factor in reducing the incidence of the disease in the U.S.S.R. by 56% during the 4 years ending on July 1, 1957.

Percutaneous vaccination, similar to that used for smallpox, is recommended. The incidence of the disease in a group of 3,000 persons thus vaccinated was 2½ times less than in similar groups vaccinated by means of subcutaneous injections, and was 7 to 11 times less than in non-vaccinated persons. The percutaneous method of vaccination is easy to perform and gives rise to very few and insignificant reactions, whereas with subcutaneous inoculation the incidence of local reactions reached 56%, and in 8% of cases a severe general reaction was reported. In addition, percutaneous vaccination does not call for preliminary testing for hypersensitivity. During 1956 and the first half of 1957 in Kazakhstan 470,574 individuals were vaccinated percutaneously without a single case of severe general reaction being observed. Other methods of prevention include sanitary and veterinary measures, follow-up of patients and contacts, and search for new cases.

S. W. Waydenfeld

INDUSTRIAL MEDICINE

786. **The Development of Standards for Environmental Hygiene in the Deep Mines of the Donbass.** (Материалы к гигиеническому обоснованию микроклимата в глубоких шахтах Донбасса)

A. A. ŠARTALA. *Гигиена Труда и Профессиональные Заболевания* [Gig. Truda prof. Zabolev.] 3, 3-8, March-April, 1959. 4 figs., 8 refs.

The current safety regulations in the coal mines of the U.S.S.R. stipulate a maximum air temperature of 25° C., with a ventilation air flow of not less than 2 m. per second. These figures have been derived from general industrial factors and are not based on research specifically carried out in deep mines. The author has therefore undertaken investigations in the deep mines of the Donbass coalfield in order to obtain the necessary data for the provision of rational standards of ventilation and temperature for such mines. The air temperature at the coal face in this coalfield may be as high as 35° C., while the relative humidity is constantly high (85 to 100%) and cannot easily be reduced by the methods available underground. The collection of comparable data was also rendered difficult by the conditions of work, which made it impossible to maintain a uniform air velocity at any point throughout a shift.

Investigations were carried out underground on 8 coal fillers with not less than 12 months' underground experience who were working at the rate of 300 kg. m. per minute wearing cotton overalls. Pulse, blood pressure, skin and body temperatures, sweat production, oxygen demand, and other factors were studied. The results showed that the temperature-regulating mechanism is subjected to perceptible strain at air temperatures of 29° C. and over and that this is not alleviated by increasing the air velocity. At 26° C. the air velocity required to produce satisfactory working conditions was not less than 2 m. per second and at 28° C. not less than 3 m. per second.

It is concluded that if the air temperature in a deep mine exceeds 28° C. with all available ventilation some form of refrigeration is essential.

Basil Haigh

787. **A Comparison of the Results of Pulmonary Function Tests with the Actual Performances of Miners at Work.** (Confrontation des résultats de l'exploration fonctionnelle pulmonaire avec le travail réellement effectué dans les mines par les ouvriers)

C. DALLOZ, L. F. PERRIN, and J. RABAULT. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [Arch. Mal. prof.] 20, 137-147, March-April, 1959.

Physiological tests of ventilating capacity as a measure of pulmonary function are increasingly relied upon in the assessment, for compensation purposes, of the impairment of capacity for work caused by pneumoconiosis. But, the authors point out, the conditions under which these tests are carried out differ widely from those which exist in performing the actual work. Besides, there may be psychological effects which follow the diagnosis of the disease and which variously influence the attitude

to work of different individuals. Environmental conditions, too, vary widely between one place of work and another.

At the Institute of Industrial Medicine, Lyons, 100 working miners [presumably coal-miners] suffering from silicosis were subjected to various physiological tests of respiratory function, these including measurement of vital capacity and maximum voluntary ventilation per second at rest and following exercise on a bicycle ergometer; the results were assessed as a percentage of a theoretical normal value. In addition the mine engineer recorded, according to a specially devised questionnaire, the actual performance of each man at work and his opinion of the difficulty of the work. Attention is particularly directed to the fact that healthy miners [possibly because of self-selection for mining] frequently have ventilation levels substantially higher (105 to 120%) than the theoretical normal, so that values below normal represent not a slight but a substantial diminution, which is particularly significant in relation to the heavy work of mining. The estimates to be made by the engineer proved difficult in performance and were definite in only 33 of the 100 cases. In some cases he confirmed the laboratory findings, but in others he differed from them, thus in the authors' view underlining the need for further investigations.

A. Meiklejohn

788. **Tuberculopneumoconiosis and Tuberculosis in Persons Exposed to Dust.** (Les tuberculo-pneumoconioses et la tuberculose des empoussiérés)

P. GALY, J. BÉRARD, and E. BAILLY. *Revue de tuberculose et de pneumologie* [Rev. Tuberc. (Paris)] 23, 1-21, Jan. [received May], 1959. 16 figs., bibliography.

This study from the Institute of Industrial Medicine and the Hôpital Belle-Vue (Saint-Etienne), Lyons, is based upon the examination of 40 lung specimens from coal-miners and others exposed to silicotic risk who required surgical treatment for resistant tuberculosis and of 50 necropsy specimens from similar patients. The authors describe a form of combined lesion of tuberculosis with pneumoconiosis which is distinct from the usual tuberculous infection superimposed upon or associated with silicosis. The basic lesion appears to be the tuberculopneumoconiotic nodule, composed of central caseation, fibrous tissue, and coal-dust particles distributed centrally as well as at the periphery. The previous lung structure is still recognizable in sections treated with special stains. The nodule is surrounded by dense fibrous tissue with hyaline changes. Epithelioid and giant cells are rarely seen. These nodules tend to conglomerate and there is a tendency to cavitation of the solid lesions and deformity of the bronchi, with occasional perforation by lymph nodes. Radiologically, the lung fields may be clear or sometimes reticular, or there may be diffuse silicotic nodules or even massive silicosis. These lesions may appear after 10 or 12 years' exposure to dust, but sometimes after much shorter intervals. Bacteriological proof of their tuberculous nature may be delayed for some years after their appearance. Response to chemotherapy or collapse therapy is frequently disappointing.

I. Ansell

789. Statistical Analysis of the 249 Fatal Cases of Malignant Pneumoconiosis Occurring during the First Ten Years of Inclusion of the Disease under Industrial Health Insurance in Italy (1943-1953). (Rilievi su 249 casi di pneumoconiosi maligna deceduti nel primo decennio di tutela assicurativa (1943-1953))

W. PAOLINO and L. TRONZANO. *Minerva medica* [Minerva med. (Torino)] 50, 978-982, April 4, 1959. 14 refs.

In this paper from the University of Turin 236 fatal cases of silicosis and 13 of asbestosis occurring in the Piedmont region during a 10-year period (1943-53) are analysed according to cause of death, type of work, length of time exposed to risk, survival time after diagnosis, and incidence of pulmonary tuberculosis. In addition, the assessment of invalidity for insurance purposes is compared with survival time.

The cases of silicosis were classified as follows: Grade I (fibrosis with little or no micronodulation), 12; Grade II (nodular), 94; Grade III (massive), 39; Grade IV (silicotuberculosis), 91. Seven of the cases of asbestosis were classified as asbestotuberculosis. The average duration of exposure to risk was 18 years for both asbestosis and silicosis, but all those cases in which the diagnosis was made within 5 years of first exposure were found in the occupations most exposed to risk; moreover, in two-thirds of these cases tuberculosis was present at the time of ascertainment of pneumoconiosis. The age on diagnosis (when known) was less than 40 years in 34 cases, 41 to 50 years in 101, 51 to 60 years in 57, and over 60 years in 25. The average survival time from diagnosis was 1.9 years for asbestosis and 3.6 years for silicosis, but it was notably shorter in the youngest age group and in all cases in which tuberculosis was present. Death was due to cardio-respiratory insufficiency in 72 of the 249 cases, to pulmonary tuberculosis in 156, to bronchopulmonary infection in 17, to miscellaneous causes in 3, and to cancer of the lung in only one (a case of Grade-I silicosis). Tuberculosis was the stated cause of death in the 7 cases of asbestotuberculosis and in 5 cases of Grade-I, 45 of Grade-II, 9 of Grade-III, and 90 of Grade-IV silicosis. The average survival time was 5 years in 33 cases in which the assessment of disability for compensation was less than 40%, 4.2 years in 79 cases in which the assessment was 40 to 69%, and 2.7 years in 100 cases in which the assessment was more than 69%.

[In the earlier part of the period the figures must inevitably have been influenced by the war, since it is likely that the population at risk then contained an abnormally higher proportion of the less physically fit and older workers. However, the high incidence of associated tuberculosis is none the less noteworthy.]

W. K. Dunscombe

790. The Chemotherapy of Poisoning by Organophosphate Anticholinesterases. [Review Article]

D. R. DAVIES and A. L. GREEN. *British Journal of Industrial Medicine* [Brit. J. industr. Med.] 16, 128-134, April, 1959. 1 fig., bibliography.

791. Intoxication with Nitro Derivatives of Glycol. (L'intossicazione da nitroderivati dei glicoli)

I. MACCHERINI and E. CAMARRI. *Medicina del lavoro* [Med. d. Lavoro] 50, 193-201, March, 1959. 29 refs.

The nitro derivatives of chief industrial importance are nitroglycerin and nitroglycol, the latter especially in the production of anti-freeze dynamite. Nitroglycerin is a heavy, oily liquid, occupational exposure to which is known to cause acute vasomotor disturbances—flushing, paraesthesiae of the extremities, headache, profuse perspiration, visual disturbance, and more rarely nausea and vomiting—and chronic effects in the form of skin lesions, loss of weight, pallor, respiratory catarrh, and hypotension. In contrast, nitroglycol is a highly volatile liquid. Absorption is chiefly by inhalation, but it can also take place through the skin. Cases of sudden and fatal collapse have occurred in persons employed for long periods in contact with nitroglycol, especially on returning to work after a holiday, and in whom necropsy has revealed no cardiac lesion. In non-fatal cases of nitroglycol intoxication the initial symptoms are those of vasomotor disturbance; these tend to decrease or disappear within 2 or 3 weeks, but are sometimes followed by psychic disturbance, a moderate increase in the nervous reflexes, and acrocyanosis. Anginal attacks with pain radiating down the left arm, usually lasting only a few minutes but sometimes repeated at short intervals, have also been described.

In a study of 265 workers employed in the production of anti-freeze dynamite the authors found that almost all complained of headache, palpitation, nausea, and a feeling of heat in the face and extremities, present on starting work but gradually diminishing with continued exposure. Of 70 workers in direct contact with nitroglycol, 10 had had anginal attacks. These usually occurred 40 to 60 hours after the cessation of work, lasted only a few minutes, and were not severe enough to warrant suspension; clinical examination gave negative results. The blood pressure, measured during working hours, was 5 to 20 mm. Hg below normal in 51.6% of all workers; electrocardiograms showed no deviation from the normal; chest radiography showed only moderate signs of arteriosclerosis in 9 subjects; moderate anaemia and leucopenia were present in a few cases, but no methaemoglobinaemia or Heinz bodies. The serum cholesterol, lipoprotein, and bilirubin levels were also within normal limits and there was no evidence of hepatic dysfunction except for a slightly positive Takata-Ara reaction in 9 persons.

It is considered that the toxic phenomena associated with exposure to nitro compounds are usually due to the combined effects of nitroglycerin and nitroglycol, the latter being especially responsible for the coronary insufficiency causing anginal crises and, occasionally, sudden death. Its mechanism of action remains obscure, but the authors suggest that during exposure the capacity of the myocardium to utilize oxygen is impaired and that an increase in oxygen consumption, not compensated for by an adequate coronary flow, occurs on cessation of exposure.

Ethel Browning

Anaesthetics

792. **Trimeprazine Tartrate for Premedication of Children**
R. W. COPE and W. J. GLOVER. *Lancet [Lancet]* 1, 858-860, April 25, 1959. 9 refs.

The authors discuss the premedication of children aged $3\frac{1}{2}$ to 7 years; they consider that children in this age group are too old for basal narcosis with rectal thiopentone and that sedation with safe doses of papaveretum and scopolamine (hyoscine) is likely to be inadequate. In this paper from the Hospital for Sick Children, Great Ormond Street, London, they report a comparative study of trimeprazine tartrate and quinalbarbitone. Trimeprazine is a newly-developed phenothiazine derivative which may be regarded pharmacologically as intermediate between promethazine and chlorpromazine, having considerable antihistaminic and anti-emetic action. A double-blind trial was precluded by the differences in bulk and taste of the two drugs, which were given by mouth; however, the assessor at least did not usually know which drug had been administered. The two drugs were given alternately to a total of 200 children, 160 undergoing tonsillectomy and 40 operations for the correction of strabismus. Trimeprazine syrup proved to be more acceptable to the children than the unpleasant-tasting barbiturate. In each series there was little difference in the degree of unconsciousness or cooperation on arrival in the anaesthetic room. Just over 50% in each series were lightly asleep, 25 to 30% were cooperative whether awake or drowsy, and 13% were uncooperative. After operation the children given trimeprazine recovered slightly more quickly, had a lower incidence of vomiting, and required less sedation than those given quinalbarbitone. These differences, however, were not statistically significant. [The drug clearly shows promise and merits further trial.]

J. F. Nunn

793. **Hypotension during Obstetrical Anesthesia**
R. L. KENNEDY, D. L. FRIEDMAN, D. M. KATCHKA, S. SELMANTS, and R. N. SMITH. *Anesthesiology [Anesthesiology]* 20, 153-155, March-April, 1959. 4 refs.

It is stated that when a patient in late pregnancy lies in the supine position obstruction of the inferior vena cava from compression by the uterus may occur. As a result the venous return to the heart is obstructed, which in turn lowers cardiac output. The pulse rate increases, the blood pressure falls, and the patient appears to be shocked. The obstruction is relieved by turning the patient on her side. Just before delivery when the patient is placed in the lithotomy position a similar situation exists. "Since the patient cannot be turned on her side at this time" [why not?] the uterus is manually displaced to the left to relieve the compression.

In an attempt to determine the frequency with which the hypotension previously considered to be due solely to spinal anaesthesia was really a manifestation of the supine hypotensive syndrome the authors, at Toledo

Hospital, Ohio, studied 600 consecutive cases in which delivery was carried out under spinal anaesthesia. Hypotension occurred in 106 (17.7%), and left uterine displacement was effective in restoring the blood pressure to normal in 99 (93%) of these patients.

W. Stanley Sykes

794. **Severe Head Injuries**
J. G. MATHESON, C. W. THOMSON, and J. D. WHITBY. *Anaesthesia [Anaesthesia]* 14, 168-177, April, 1959. 1 fig., 17 refs.

The part which the anaesthetist can play in the management of patients who are unconscious following head injury is discussed in this paper from Newcastle General Hospital. It is advocated that upon admission of the patient to hospital a thorough tracheal toilet should be carried out, followed by routine endotracheal intubation. The indications for tracheotomy are described and also the management of the patient thereafter. The "lytic cocktail" is useful for producing sedation and assisting cooling when this is necessary for the maintenance of a normal temperature. The authors emphasize the importance of supervision of the fluid balance and the avoidance of cerebral oedema, and discuss the dangers of relapse during the second week.

Mark Swerdlow

795. **A Clinical Trial of Dihydrohydroxycodone Pectinate**
R. H. BOYD. *Anaesthesia [Anaesthesia]* 14, 144-147, April, 1959. 5 refs.

The efficacy of dihydrohydroxycodone ("proladone") for premedication and postoperative analgesia was studied in 297 patients at St. Margaret's Hospital, Epping. To 47 patients 10 mg. of proladone with 50 mg. of chlorpromazine and 0.6 mg. of hyperduric atropine was given by intramuscular injection one hour before operation. Of these, 39 appeared to be more awake one hour later than would have been expected with the usual premedication, but the majority were not visibly apprehensive. Most of the patients required more anaesthetic drugs than after standard premedication.

Proladone was the sole agent for the relief of postoperative pain in 250 patients subjected to a wide variety of surgical procedures. It was given by intramuscular injection in a dose of 10 to 20 mg., no patient receiving more than 3 doses. Satisfactory analgesia was obtained in 229 (91.6%) of the patients. Relief was effective within 25 to 30 minutes and lasted for some 6 to 10 hours. Side-effects were minimal and return of consciousness was not delayed. The maximum benefit was obtained when the drug was injected 30 minutes before the end of the operation.

[A double-blind technique was not employed, nor was there a placebo control group.]

Mark Swerdlow

Radiology

RADIODIAGNOSIS

796. **The Angiocardiographic Diagnosis of Mitral Insufficiency. Value of the Retrograde Percutaneous Arterial Route.** (Le diagnostic angiocardiographique de l'insuffisance mitrale. Intérêt de la voie artérielle percutanée rétrograde)

M. MOUQUIN, E. CHARTRAIN, P. BRUN, J. Y. PIERRON, and G. BACQUET. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [Bull. Soc. méd. Hôp. Paris] 75, 285-292, March, 1959. 4 figs.

It is pointed out that of all the numerous signs and procedural findings indicative of mitral stenosis, no single one is an absolute criterion. For this reason the authors, working at the Hôpital Broussais, Paris, have investigated in 32 cases the value of radiological visualization of mitral regurgitation by left ventricular angiography by the percutaneous route, the apparatus used being a considerably modified version of that of Seldinger.

The pressure of the injection brings the tip of the catheter against the ventricular wall. In the normal heart it is only if the tip of the catheter is directed towards the left auricle that opacification of this chamber may occur, and it then appears in the first films, whereas in mitral regurgitation opacification of the ventricle always precedes that of the auricle. Extrasystoles do not prevent the ventricle from functioning normally. In contrast, in cases of mitral stenosis without regurgitation not even the slightest reflux of the opaque medium is observed. By this method calcification of the mitral valve may sometimes be noted. In 9 cases of mitral stenosis with reflux or of simple insufficiency regurgitation into the left auricle occurred on each occasion following opacification of the ventricle. The authors consider that the method should be employed as a routine at all specialized centres, and state that in their hands it has presented no particular difficulty and carried no risk in over 100 cases.

John H. L. Conway-Hughes

797. **The Roentgen Diagnosis and Management of Prepyloric Narrowings**

R. S. SHERMAN, YING-MING YEN, L. BOWDEN, and H. M. SELBY. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [Amer. J. Roentgenol.] 81, 582-598, April, 1959. 11 figs., 28 refs.

The results of this study of 23 histologically proved and roentgenologically similar prepyloric narrowings, 17 benign and 6 malignant, indicate that there is a definite inherent limitation in the roentgen diagnosis of lesions of this type. Experienced radiologists when tested with some of this material offered diagnoses that were largely incorrect and not based upon factual knowledge. The only roentgen appearance of possible

diagnostic significance was the faint, double edge or margin found in 2 of the 6 cancer cases.

These prepyloric narrowings constitute one type of gastric lesion for which cytologic help would be especially valuable. When the surgeon described the stomach as normal or when only scarring was present, the final pathologic diagnosis was always benign. When some degree of thickening or a mass was noted, the final diagnosis was as likely to be cancer as not. Present day surgical diagnosis entails gastrotomy, inspection, and full thickness biopsy in all cases that do not present typical induration or mass. Perhaps all of these patients showing achlorhydria should be resected.

A better correlation between the roentgenologic and pathologic findings in the lesions being discussed is needed, but apparently the pathologic definition of the normal and a number of benign conditions in the prepyloric region is not standardized or always consistent. Follow-up studies are indicated to determine fully the eventual course of the benign prepyloric narrowings unassociated with gastric retention and decompensation that are not treated surgically.—[Authors' summary.]

798. **Oral Cholangiography. A Method of Visualizing the "Nonvisualized" Gallbladder**

J. R. TWISS and L. GILLETTE. *Journal of the American Medical Association* [J. Amer. med. Ass.] 169, 1275-1278, March 21, 1959. 6 figs., 7 refs.

This paper reports the results obtained with the authors' technique of oral cholangiography in 46 cases after routine cholecystography had failed to demonstrate satisfactorily the gall-bladder or common bile duct. The evening before examination patients had supper at 6 p.m., and at 7 p.m. were given 6 tablets of "telepaque" (iopanoic acid) with a glass of water; this dose was repeated after 30 minutes. At 9 p.m. a teaspoonful of paregoric was administered in a glass of water. Next morning no breakfast was allowed, but at 7 a.m. 6 more tablets of telepaque were given, and at 9 a.m. 2 teaspoonfuls of paregoric in a little water. Radiographs were taken at 10 a.m., 11 a.m., and noon, and again 24 hours later if visualization of the gall-bladder or bile duct was not successful.

Satisfactory demonstration of the gall-bladder was obtained in 33 of the 46 cases, and the common bile duct was shown in a further 6. Stones were present in 23 of the cases in which the gall-bladder or common duct was visualized; in 18 of these operation was performed, the diagnosis being confirmed in 17. In 12 cases the gall-bladder without stones was demonstrated, but the common duct was not seen. Of this group, only 3 were operated on, and all 3 had obstruction of the common bile duct. No gall-bladder shadow was detected in 11 cases, but in 6 of them the common duct was visible, in 2 cases containing stones. Operations

were performed on 8 of the 11 patients, and in all cases obstruction of the cystic duct from various causes was found. Normal gall-bladder function was found on 9 occasions and the patients were thus spared surgical intervention.

The authors claim that this technique offers a method of differentiating pathological conditions in which conventional cholecystography may show only non-function or poor function of the gall-bladder. In cases of mild catarrhal cholecystitis gall-bladder function may be shown to be normal by this technique and the patient thus spared an operation, while complete obstruction of the cystic duct does not permit visualization of the gall-bladder by any method of cholangiography. Many cases of cholelithiasis or chronic cholecystitis with choledocholithiasis can be positively diagnosed pre-operatively by oral cholangiography even when no results are obtainable by the intravenous method. It is suggested that oral administration of opaque medium should be tried in all cases in which routine cholecystography has failed.

Arnold Appleby

799. An Evaluation of the Roentgen Changes in Acute Pancreatitis: Correlation with Clinical Findings

G. N. STEIN, M. H. KALSER, N. N. SARIAN, and A. FINKELSTEIN. *Gastroenterology* [*Gastroenterology*] 36, 354-361, March, 1959. 3 figs., 15 refs.

In a review of the literature the authors have found that no fewer than 23 possible radiological abnormalities have been reported as occurring in acute pancreatitis, but no methodical attempt has apparently been made to determine the relative frequency of such signs. In an effort to repair this omission they have reviewed the radiographs of 66 patients admitted to the Graduate Hospital of the University of Pennsylvania, Philadelphia, for 73 separate episodes of acute pancreatitis.

The plain film of the abdomen showed a "sentinel loop" in 34 out of 61 radiographic investigations; this appears as an abnormally gas-distended loop or loops of small intestine in the left mid-abdomen, in some cases extending into the left upper abdomen and occasionally across the midline to the right abdomen. Pancreatic calculi or calcification was noted in 10 (17%) of these 61 plain films, and is considered an important diagnostic sign. A study of the radiographs of the chest in 40 cases revealed that in one there was a pleural effusion, while 18 showed elevation of the diaphragm or plate-like atelectasis, usually on the right side only. The only significant finding on barium-meal examination, which was carried out on 43 occasions, was the demonstration of an enlarged papilla of Vater in 10 cases. Cholecystography, performed on 51 patients, showed that the gall-bladder was normal in 31 cases, contained calculi but was functioning normally in 15, was poorly visualized in one, and failed to opacify in 4.

Apart from these findings no other radiological abnormalities were encountered with any frequency. There seemed to be little association between the type of pancreatitis (or its presumed aetiology) and the radiological findings, except for the rarity of gall-bladder disease in

those cases in which the aetiology was considered alcoholic; here, however, the final diagnosis may well have been influenced by the radiological findings. The authors conclude that the most reliable radiological evidence of acute pancreatitis is the demonstration of pancreatic calcification in association with the presence of a "sentinel loop".

T. D. Kellock

800. Intravenous Urography with Renografin 60%. A Report of More Than 600 Cases

L. M. ORR, J. L. CAMPBELL, and M. W. THOMLEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 169, 1156-1158, March 14, 1959. 7 refs.

The reliability and safety of intravenous urography were studied in 654 patients. The injection consisted of 25 c.cm. of "renografin" (a 60% aqueous solution of the methylglucamine salt of 3:5-diacetyl-amido-2:4:6-triiodobenzoate) given over a period of three minutes; in only 3 cases were smaller doses used. There were no severe reactions, but vomiting occurred in 11 patients. One of these had a history of allergy, and another had not been properly prepared. The low incidence of reactions was striking because the ages of the patients ranged from 7 to 84 years and 16 had histories of allergy or severe reactions to previously administered contrast agents. Satisfactory roentgenograms of the kidneys were obtained in 636 (97%) of the cases, demonstrating the great diagnostic value of this procedure.—[Editorial summary.]

RADIOTHERAPY

801. Supervoltage (2 MeV.) Rotation Irradiation of Carcinoma of the Head and Neck

M. FRIEDMAN, M. E. SOUTHARD, and W. ELLETT. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] 81, 402-419, March, 1959. 17 figs., 5 refs.

The authors describe, from the Hospital for Joint Diseases, New York, their treatment of 147 tumours in 143 patients with carcinoma of the head and neck seen between 1951 and 1957. All were treated with x rays from a 2-MeV. resonant transformer generator. Of the 147 tumours, most of which were squamous-cell carcinomata, 98 were treated by means of rotation techniques and 49 using stationary fields. The majority of the carcinomata were extensive, less than 10% being under 3 cm. in diameter, and 45% were recurrent after previous irradiation or surgery. It was shown that four basic rotation patterns sufficed for almost all the lesions. For tumours at certain sites, such as the larynx, it was found that the rotation technique had no advantage over fixed fields and so was not used. After 16 cases of carcinoma of the anterior two-thirds and margin of the tongue had been treated by supervoltage, mostly with rotation, it was concluded that this method was inferior to interstitial implantation and it was therefore abandoned.

The doses used were considerably higher than equivalent doses in conventional therapy, 6,500 to 10,000 rads being found necessary to produce results comparable to

those obtained with 6,000 rads at conventional voltage. It was expected that the incidence of radionecrosis in bone would be less than that with 250-kV. x rays, but this was found not to be so, as 10 patients developed such radionecrosis, of whom 5 had received previous irradiation with 200-kV. x rays. In 21 cases of carcinoma of the tonsil, mostly treated with rotation technique, all the lesions primarily regressed, while 12 were arrested for periods of one to 5 years. Other lesions effectively arrested were carcinoma of the posterior third of the tongue and recurrent carcinoma of the larynx. In this whole series of cases of advanced carcinoma of the head and neck treated with 2-MeV. irradiation the over-all apparent arrest rate was 33% at 3 years and 29% at 5 years.

K. S. Holmes

802. Comparison of Medium Voltage and Supervoltage Roentgen Therapy in the Treatment of Oropharynx Cancers

G. H. FLETCHER, W. S. MACCOMB, P. M. CHAU, and W. G. FARNSLEY. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [Amer. J. Roentgenol.] 81, 375-401, March, 1959. 13 figs., 8 refs.

This paper from the M.D. Anderson Hospital and Tumor Institute, Houston, Texas, deals with the treatment of malignant tumours at two sites: (1) the palatine arch, comprising the retromolar trigone, anterior faucial pillars, and soft palate, and (2) those of the oropharynx, comprising the tonsils, base of the tongue, and pharyngeal walls; lymphomata and tumours of salivary origin were excluded. Staging was based on size of the primary tumour and on the extent of metastases in the regional lymph nodes at any time or of distant metastases when first seen, and classified as "favourable", "moderately favourable" and "very unfavourable". The tumours treated by supervoltage were on the whole more advanced than those treated by conventional radiotherapy. In view of the advanced age of many of the patients in the series, as well as the development of early metastases and the common occurrence of intercurrent fatal disease, the usual criterion of 5-year survival was not applied and the analysis was based on the degree of control of the primary tumour or of metastases in lymph nodes and of survival at 1, 2, and 3 years. Treatment policy is described, with details of the varying techniques applied with both supervoltage and conventional radiotherapy. (Numerous helpful diagrams and case histories are presented to illustrate some of the techniques used.)

The conclusions drawn are that for cancer of the palatine arch supervoltage radiotherapy probably gives better control, although the small numbers involved and the non-comparability of the cases make definite conclusions difficult. As regards tumours of the oropharynx all sub-groups showed a more definite improvement in control, and this was reflected by a statistically significant increase in the numbers of survivors at 1, 2, and 3 years. In considering radiation reactions it was decided, for the sake of uniformity, to use those occurring on the mucous membrane of the soft palate; on this basis the relative biological effectiveness of 3 mm. Cu half-value layer as compared with supervoltage irradiation was deduced to

be 0.85 to 0.9. The management of local recurrences and complications and the treatment of neck lymph nodes are discussed. It is interesting that the authors' estimate of the safe dose to avoid producing transverse myelitis in carrying out irradiation of the neck with long parallel opposing fields is one of 5,000 r. given over 4 to 6 weeks.

F. Kelly

803. The Rapid Palliative Treatment of Breast Carcinoma. A Preliminary Report

D. Q. COCHRAN, S. HOLTZ, and W. E. POWERS. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [Amer. J. Roentgenol.] 81, 479-484, March, 1959. 7 figs., 10 refs.

Writing from the Mallinckrodt Institute of Radiology (Washington University School of Medicine), St. Louis, the authors describe the palliative treatment of 17 cases of carcinoma of the breast, in all of which there were either distant metastases or advanced primary lesions and fixed regional nodes when first seen. They suggest that irradiation is an effective method of palliation and that rapid local control can be obtained without major complications or morbidity with doses of the order of 2,000 r. given in 2 days to the tumour and its metastatic nodes, delivered as high-voltage radiation in order to ensure 90% homogeneity. In the present series irradiation was carried out by means of a betatron producing x rays of 22.5 MeV. energy. Most of the patients were subjected to castration with or without hormone therapy in addition to irradiation.

The primary tumours were irradiated by means of tangential medial and lateral ports which included the breast, chest wall, and part of the underlying lung; the internal mammary nodes were not included in these fields. The supraclavicular, infraclavicular, and axillary lymph-node areas were treated by directly opposing anterior and posterior ports which joined the upper part of the tangential fields, the field sizes being 15×15 or 12×15 cm. The tumour dose given was initially 1,250 r. in 2 days, but this was subsequently increased to 2,500 r. in 2 days. The entire treatment was given in 4 consecutive days. Follow-up of 15 available cases showed that 8 patients, all with distant metastases before therapy, had died, but in the 7 survivors the primary tumour and involved supraclavicular and axillary lymph nodes had either definitely regressed or completely disappeared; in none of these cases has local recurrence been noted. Four patients developed radiographic evidence of pulmonary fibrosis, mainly in the apex, but none had symptoms.

F. Kelly

804. Eight Further Cases of Radiation-induced Cancer

M. GARRET. *British Medical Journal* [Brit. med. J.] 1, 1329-1331, May 23, 1959. 1 fig., 15 refs.

Another 8 cases of radiation-induced laryngeal and pharyngeal carcinomata are reported. All the patients were previously treated for thyrotoxicosis. Among the 8 cases is a carcinoma of the vocal cord, bringing to 6 the number of true laryngeal carcinomata assumed to be radiation-induced and reported in the literature.—[Author's summary.]